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TRANSACTIONS

OF THE

ASSOCIATION OF AMERICAN PHYSICIANS.

NINTH SESSION,

HELD AT WASHINGTON, D. C.,

MAY 29, 30, 31, AND JUNE 1, 1894.

VOLUME IX.

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ASSOCIATION OF AMERICAN PHYSICIANS

OFFICERS FOR THE YEAR 1894–95.

PRESIDENT.

WILLIAM OSLER, M.D.

VICE–PRESIDENT.

A. JACOBI, M.D.

RECORDER.

I. MINIS HAYS, M.D.

SECRETARY.

HENRY HUN, M.D.

TREASURER.

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JOHN H. MUSSER, M.D.
J. E. GRAHAM, M.D.

REPRESENTATIVE ON THE EXECUTIVE COMMITTEE OF THE CONGRESS OF AMERICAN PHYSICIANS AND SURGEONS.

WILLIAM H. WELCH, M.D.

ALTERNATE REPRESENTATIVE.

M. ALLEN STARR, M.D.

HONORARY MEMBERS.

† Deceased.

†1890. Barker, Fordyce, M.D., New York.
1886. Billings, John S., M.D., U. S. A., Surgeon-General's Office, Washington, D.C.
†1886. Bowditch, Henry I., M.D., Boston.
†1886. Clark, Alonzo, M.D., New York.
1886. Clymer, Meredith, M.D., 65 W. 38th St., New York.
†1886. Dalton, John C., M.D., New York.
†1886. Leidy, Joseph, M.D., Philadelphia.
1886. Metcalfe, John T., M.D., 30 W. 33d St., New York.
1886. Minot, Francis, M.D., 65 Marlborough St., Boston.
1886. Stillé, Alfred, M.D., 3900 Spruce St., Philadelphia.

MEMBERS.

* Original members.
† Deceased members.

1892. Abbott, Alexander C., M.D., Laboratory of Hygiene, University of Pennsylvania, Philadelphia.
1894. Adami, J. George, M.D., Pathological Laboratory, McGill University, Montreal, Canada.
*1886. Adams, J. F. A., M.D., 26 Wendell Ave, Pittsfield, Mass.
*1886. Atkinson, I. E., M.D., 605 Cathedral St., Baltimore.
*1886. Ball, A. Brayton, M.D., 42 W. 36th St., New York.
*1886. Baumgarten, G., M.D., 2643 Chestnut St., St. Louis.
1894. Biggs, Herman M., M.D., 5 W. 58th St., New York.
1892. Bolton, Meade, M.D., Pathological Laboratory, Johns Hopkins University, Baltimore.
1890. Bond, Charles S., M.D., 112 N. 10th St., Richmond, Indiana.
1888. Bridge, Norman, M.D., 217 S. Broadway, Los Angeles, California.
†1886. Bruen, Edward T., M.D., Philadelphia.
*1886. Busey, Samuel C., M.D., 1545 I St. (N. W.), Washington, D. C.
1889. Cary, Charles, M.D., 340 Delaware Ave., Buffalo, N.Y.
*1886. Chew, Samuel C., M.D., 215 W. Lanvale St., Baltimore.
*1886. Councilman, William T., M.D., Harvard Medical School, Boston.
1894. Cutler, Elbridge G., M.D., 214 Beacon St., Boston.
1889. Dabney, William C., M.D., University of Virginia, Va.
*1886. Da Costa, J. M., M.D., 1700 Walnut St., Philadelphia.
1888. Dana, Charles L., M.D., 50 W. 46th St., New York.
*1886. Dana, Israel T., M.D., 181 State St., Portland, Me.
1888. Danforth, I. N., M.D., 294 W. Monroe St., Chicago.

*1886. Delafield, Francis, M.D., 12 W. 32d St., New York.
1893. Dock, George, M.D., University of Michigan, Ann Arbor, Mich.
†1886. Donaldson, Frank, M.D., Baltimore.
*1886. Draper, William H., M.D., 19 E. 47th St., New York.
*1886. Edes, Robert T., M.D., Adams Nervine Asylum, Jamaica Plain, Mass.
1888. Ernst, Harold C., M.D., Jamaica Plain, Mass.
1890. Fisk, Samuel A., M.D., 37 18th Ave., Denver, Col.
*1886. Fitz, Reginald H., M.D., 18 Arlington St., Boston.
*1886. Folsom, Charles F., M.D., 15 Marlborough St., Boston.
*1886. Forchheimer, F., M.D., 160 W. 9th St., Cincinnati.
†1886. Formad, Henry F., M.D., Philadelphia.
1894. Fussell, M. Howard, M.D., 189 Green Lane, Manayunk, Philadelphia.
*1886. Garland, George M., M.D., 274 Newbury St., Boston.
†1889. Geddings, W. H., M.D., Aiken, S. C.
*1886. Graham, J. E., M.D., Gerrard St., Toronto, Canada.
1890. Griffith, J. P. Crozer, M.D., 123 S. 18th St., Philada.
*1886. Guitéras, John, M.D., 3731 Spruce St., Philadelphia.
1890. Hare, Hobart A., M.D., 222 S. 15th St., Philadelphia.
*1886. Hays, I. Minis, M.D., 266 S. 21st St., Philadelphia.
*1886. Henry, Frederick P., M.D., 1635 Locust St., Philada.
†1886. Howard, R. Palmer, M.D., Montreal, Canada.
†1886. Hudson, E. Darwin, Jr., M.D., New York.
*1886. Hun, Henry, M.D., 149 Washington Ave., Albany, N. Y.
1890. Hurd, Henry Mills, M.D., Johns Hopkins Hospital, Baltimore.
†1886. Hutchinson, James H., M.D., Philadelphia.
*1886. Jacobi, A., M.D., 110 W. 34th St., New York.
*1886. Janeway, E. G., M.D., 36 W. 40th St., New York.
†1886. Johnson, Hosmer A., M.D., Chicago.
*1886. Johnston, W. W., M.D., 1603 K St. (N. W.), Washington, D. C.
*1886. Kinnicutt, Francis P., M.D., 42 W. 37th St., New York.
1890. Latimer, Thomas S., M.D., 103 W. Monument St., Baltimore.
1888. Lewis, Morris J., M.D., 1316 Locust St., Philadelphia.

*1886. Longstreth, Morris, M.D., 1416 Spruce St., Philada.
*1886. Loomis, Alfred L., M.D., 19 W. 34th St., New York.
1889. Loving, Starling, M.D., 229 E. State St., Columbus, Ohio.
*1886. Lusk, William T., M.D., 47 E. 34th St., New York.
*1886. Lyman, Henry M., M.D., 65 Randolph St., Chicago.
†1886. McBride, Thomas A., M.D., New York.
†1890. MacDonnell, R. L., M.D., Montreal, Canada.
1891. McPhedran, A., M.D., 84 College St., Toronto, Canada.
1891. Mason, A. Lawrence, M.D., 265 Clarendon St., Boston.
1887. Meigs, Arthur V., M.D., 1322 Walnut St., Philadelphia.
1892. Meltzer, S. J., M.D., 66 E. 124th St., New York.
*1886. Miles, F. T., M.D., 514 Cathedral St., Baltimore.
*1886. Mitchell, S. Weir, M.D., 1524 Walnut St., Philada.
1887. Musser, John H., M.D., 40th and Locust Sts., Philada.
1891. Northrup, W. P., M.D., 57 E. 79th St., New York.
1892. Nuttall, George H. F., M.D., Johns Hopkins University, Baltimore.
*1886. Osler, William, M.D., 1 W. Franklin St., Baltimore.
*1886. Peabody, George L., M.D., 57 W. 38th St., New York.
*1886. Pepper, William, M.D., 1811 Spruce St., Philadelphia.
*1886. Polk, William M., M.D., 7 E. 36th St., New York.
1888. Prentiss, D. W., M.D., 1101 14th St. (N. W.), Washington, D. C.
*1886. Prudden, T. Mitchell, M.D., 160 W. 59th St., New York.
*1886. Putnam, James J., M.D., 106 Marlborough St., Boston.
1894. Rachford, B. K., M.D., 117 Broadway, Cincinnati.
1887. Reeves, James E., M.D., 201 McCallie Ave., Chattanooga, Tenn.
*1886. Robinson, Beverley, M.D., 37 W. 35th St., New York.
†1886. Rochester, Thomas F., M.D., Buffalo, N. Y.
1889. Roosevelt, J. West, M.D., 32 E. 31st St., New York.
†1886. Ross, George, M.D., Montreal, Canada.
1893. Rotch, T. M., M.D., 197 Commonwealth Ave., Boston.
†1886. Schmidt, H. D., M.D., New Orleans, La.
*1886. Seguin, E. C., M.D., 47 W. 50th St., New York.
*1886. Shakespeare, Edward O., M.D., Rosemont, Pa.

*1886. Shattuck, Frederick C., M.D., 125 Marlborough St., Boston.
*1886. Shattuck, George B., M.D., 24 Marlborough St., Boston.
*1886. Sinkler, Wharton, M.D., 1606 Walnut St., Philada.
*1886. Smith, A. A., M.D., 40 W. 47th St., New York.
1891. Smith, Andrew H., M.D., 22 E. 42d St., New York.
1892. Smith, Theobald, M.D., Department of Agriculture, Washington, D. C.
1887. Starr, Louis, M.D., 1818 S. Rittenhouse Square, Phila.
1887. Starr, M. Allen, M.D., 22 W. 48th St., New York.
*1886. Sternberg, George M., M.D., U. S. A., Surgeon-General's Office, Washington, D. C.
*1886. Stewart, James, M.D., 939 Dorchester St., Montreal, Canada.
1889. Stockton, Charles G., M.D., 436 Franklin St., Buffalo, New York.
†1886. Thacher, James K., M.D., New Haven, Conn.
1889. Thompson, W. Gilman, M.D., 49 E. 30th St., New York.
1889. Thomson, William H., M.D., 7 W. 56th St., New York.
*1886. Trudeau, Edward L., M.D., Saranac Lake, Franklin Co., N. Y.
*1886. Tyson, James, M.D., 1506 Spruce St., Philadelphia.
1889. Vaughan, Victor C., M.D., University of Michigan, Ann Arbor, Mich.
1889. Walcott, Henry P., M.D., 11 Waterhouse St., Cambridge, Mass.
*1886. Ward, Samuel B., M.D., 135 N. Pearl St., Albany, N.Y.
*1886. Welch, William H., M.D., 935 St. Paul St., Baltimore.
*1886. Whittaker, James T., M.D., 100 Garfield Place, Cincinnati.
*1886. Wilkins, George, M.D., 898 Dorchester St., Montreal, Canada.
1894. Williams, Francis H., M.D., 23 Marlborough St., Boston.
*1886. Wilson, James C., M.D., 1437 Walnut St., Philadelphia.
*1886. Wood, Horatio C., M.D., 1925 Chestnut St., Philada.

ASSOCIATION

OF

AMERICAN PHYSICIANS.

CONSTITUTION

As Amended May 30, 1893.

Article I.

Object and Name.

This Association has for its object the advancement of scientific and practical medicine, and shall be known as The Association of American Physicians.

Article II.

Members.

The number of active members shall be limited to one hundred. Physicians of sufficient eminence to merit the distinction may, to a number not exceeding twenty-five, be elected honorary members, and as such shall be entitled to attend all meetings and to take part in the proceedings, but not to vote.

Membership shall lapse by reason of absence from three successive annual meetings without reason given acceptable to the Council. An excused absence shall not be regarded as an attendance. Membership may be forfeited for reasons deemed sufficient by the Association.

Article III.

Officers.

The Officers of the Association shall be a President, a Vice-President, a Secretary, a Recorder, a Treasurer—all to be elected annually;

five Councillors—one to be elected each year for a term of five years; and a Representative to serve on the Executive Committee of the Congress of American Physicians and Surgeons, to be elected at the annual meeting immediately following the Congress.

Article IV.

Duty of Officers.

The duties of the President, Vice-President, Secretary, and Treasurer shall be those usually assigned to these officers.

The Recorder shall secure the papers read and also proper notes of the discussions thereon, and shall publish the annual volume of Transactions.

The five Councillors shall constitute a Committee of Nomination of Officers, and as such shall present a report at the commencement of the morning session of the last day of the annual meeting, at the conclusion of which session the election shall be held by ballot.

The Representative on the Executive Committee of the Congress shall have full power to represent the Association on all ordinary questions, but must be authorized by the Council of this Association before assenting to the admission of any Society to the Congress.

Article V.

Council.

The officers of the Association shall constitute the Council, of which four members shall constitute a quorum. It shall be the duty of the Council to supervise the affairs of the Association, to make all the arrangements for the annual meeting, to suggest the subject for debate, and to consider the nominations for membership and report on them at the meeting at which they shall be balloted on.

Article VI.

Meetings.

1. The Association shall hold an annual meeting in the City of Washington, D. C., at a time designated by the Council.

2. The President shall call the meeting to order and open the session by an address not exceeding half an hour in length. In his absence the Vice-President shall preside, and in the absence of both these officers, the senior Councillor.

3. Then shall follow original communications, discussions on subjects of general interest in the department of medicine and pathology, demonstrations in pathology, and miscellaneous business.

4. Authors of papers, and referees and co-referees who open a discussion shall not occupy more than thirty minutes each; and in the discussion following, the remarks of each speaker shall be limited to ten minutes.

5. The referees, co-referees, and authors of papers shall send abstracts of their papers to the Council for distribution to members previous to the meeting.

Article VII.

Quorum.

Any number of members present at the appointed time of the annual meeting shall constitute a quorum for the transaction of ordinary business, but for the election of members, fifteen shall be necessary for a quorum; and for altering the Constitution, twenty-five members shall be necessary.

Article VIII.

Election of Members.

Nominations to membership, signed by two members who are not officers of the Association, must be made in writing at an annual meeting of the Association; and within six months of the time of nomination the nominators shall transmit to the Council letters stating the qualifications of the nominee, and also a list of his professional positions and publications. The Council shall report the name of each nominee to the members of the Association by letter prior to acting upon the same. The Council shall report those nominations which are approved by it to the next annual meeting for action. An affirmative vote of three-fourths of the members present shall be necessary for the election of active members, but for the election of honorary members a unanimous vote of those present shall be required.

Article IX.

Annual Dues.

The annual dues of the Association shall be such sum as the Council from time to time may fix, from the payment of which honorary members shall be exempt.

Article X.

Amendments to the Constitution.

Amendments to the Constitution must be proposed in writing by five members at an annual meeting and must be acted upon at the succeeding annual meeting, the notices for which shall contain an announcement of the proposed amendments; and such amendments shall require for their adoption an affirmative vote of three-fourths of those present.

MINUTES

OF THE

NINTH ANNUAL MEETING,

Held at Washington, D. C., May 29, 30, *and* 31, *and June* 1, 1894.

The following members were present during the meeting:

A. C. Abbott.	J. P. Crozer Griffith.	J. J. Putnam.
J. F. A. Adams.	H. A. Hare.	J. E. Reeves.
I. E. Atkinson.	F. P. Henry.	Beverley Robinson.
A. B. Ball.	Henry Hun.	J. W. Roosevelt.
J. S. Billings.	H. M. Hurd.	T. M. Rotch.
Meade Bolton.	A. Jacobi.	F. C. Shattuck.
Norman Bridge.	E. G. Janeway.	G. B. Shattuck.
S. C. Busey.	W. W. Johnston.	Wharton Sinkler.
S. C. Chew.	F. P. Kinnicutt.	A. A. Smith.
W. T. Councilman.	Morris Longstreth.	A. H. Smith.
W. C. Dabney.	A. L. Loomis.	Theobald Smith.
J. M. Da Costa.	W. T. Lusk.	Louis Starr.
C. L. Dana.	H. M. Lyman.	M. A. Starr.
I. T. Dana.	A. V. Meigs.	G. M. Sternberg.
I. N. Danforth.	S. J. Meltzer.	James Stewart.
Francis Delafield.	F. T. Miles.	C. G. Stockton.
George Dock.	J. H. Musser.	W. G. Thompson.
R. T. Edes.	W. P. Northrup.	James Tyson.
H. C. Ernst.	Wm. Osler.	V. C. Vaughan.
S. A. Fisk.	G. L. Peabody.	H. P. Walcott.
R. H. Fitz.	Wm. Pepper.	W. H. Welch.
C. F. Folsom.	W. M. Polk.	George Wilkins.
F. Forchheimer.	D. W. Prentiss.	Jas. C. Wilson.
J. E. Graham.	T. M. Prudden.	H. C. Wood.

TUESDAY, MAY 29TH.

The President, Dr. Reginald H. Fitz, called the Association to order at 10.15 A.M., and read the "President's Annual Address." (See p. 1.)

The Secretary then read a communication from the Cosmos Club, offering the hospitality of the Club to the members of the Association during the Congress, and was instructed to return to the Cosmos Club the thanks of the Association for this courtesy.

The following amendment to the Constitution was offered and laid over until the next annual meeting for action:

"We, the undersigned, offer as an amendment to the Constitution that at the end of the first sentence of Article II., the words 'and twenty-five' be added, so that the first sentence of Article II. of the Constitution shall read: 'The number of active members shall be limited to one hundred and twenty-five.' (Signed) Wm. Osler, W. W. Johnston, R. H. Fitz, Henry Hun, and J. H. Musser."

The Treasurer's report was read and referred to Drs. Tyson and Delafield as an Auditing Committee.

Dr. Beverley Robinson then read a paper entitled "The Treatment of Certain Symptoms of Croupous Pneumonia, Particularly in Adults," which was discussed by Drs. Peabody, Wilson, Vaughan, and Robinson.

Dr. S. A. Fisk read a paper entitled "A Treatment of Typhoid Fever," which was discussed by Drs. Atkinson, Folsom, Adams, Osler, Vaughan, and Fisk.

Dr. C. F. Folsom read a paper entitled "Six Cases of Traumatic Headache," which was discussed by Dr. Starr.

Dr. F. P. Henry read a paper entitled "Clinical Report of Two Cases of Raynaud's Disease," which was discussed by Drs. Lyman, Osler, Starr, Welch, and Henry.

Dr. H. C. Ernst read a paper entitled "Dr. S. C. Martin's Researches on the Bacteria of Vaccinia," which was discussed by Drs. Welch, Abbott, Sternberg, and Ernst.

Adjourned at 1.25 P.M.

Wednesday, May 30th.

The President, Dr. Reginald H. Fitz, called the Association to order at 10.10 A.M.

Dr. Theobald Smith then read a paper entitled "Modification, Temporary and Permanent, of Physiological Characters of Bacteria in Mixed Cultures," which was discussed by Drs. Sternberg, Welch, and Smith.

Dr. Meade Bolton read a paper entitled "The Effect of Various Metals on the Growth of Pathogenic Bacteria," which was discussed by Drs. Welch and Smith.

Dr. W. Gilman Thompson read a paper entitled "Note on the Obser-

vation of Malarial Organisms in Connection with Typhoid Fever," which was discussed by Drs. Osler, Kinnicutt, Peabody, Janeway, Sternberg, Wilson, Musser, Lyman, Councilman, Shattuck, Reeves, Dock, and Thompson.

Dr. George Dock read a paper entitled "Experiments in Artificial Melanosis."

Dr. Thomas M. Rotch then read a paper entitled "Some of the Chemical and Bacteriological Characteristics of Milk," which was discussed by Drs. Forchheimer, T. Smith, and Rotch.

Adjourned at 1.10 P.M.

THURSDAY, MAY 31ST.

The President, Dr. Reginald H. Fitz, called the Association to order at 10.08 A.M.

The Auditing Committee reported that they had examined the Treasurer's report and vouchers, and had found them correct. The report was accepted and the Committee discharged.

Dr. J. P. Crozer Griffith read a paper entitled "Tetany in America, with a Report of Five Cases," which was discussed by Drs. Thompson, Janeway, Stockton, Jacobi, Osler, Putnam, Stewart, and Griffith.

Dr. Kinnicutt then presented several blood charts of cases of leucocytosis.

Dr. Wharton Sinkler read a paper entitled "Lead Palsy in Children," which was discussed by Drs. Putnam and M. A. Starr.

Dr. C. L. Dana read a paper entitled "A Study of the Temperature in Cerebral Apoplexy," which was discussed by Drs. Putnam, Stockton, and Dana.

Dr. John H. Musser read a paper entitled "The Mild Character and Diminished Prevalence of Syphilis and the Infrequency of Visceral Syphilis," which was discussed by Drs. Janeway, Lyman, Atkinson, and Post.

Dr. F. C. Shattuck read a paper entitled "The Frequency of Renal Albuminuria, as Shown by Albumin and Casts, Apart from Bright's Disease, Fever, or Obvious Cause of Renal Irritation," which was discussed by Dr. Danforth.

Dr. T. M. Prudden then gave a demonstration by specimens and photographs of "Experimental Phthisis in the Rabbit with Formation of Cavities."

In the absence of Dr. Trudeau, his paper, entitled "A Report of the Ultimate Results Obtained on Experimental Eye Tuberculosis by Tuber-

culin Treatment and Anti-tubercular Inoculation," was read by Dr. Loomis.

Dr. N. Bridge read a paper entitled "Cough Aggravated by Horizontal Posture on One Side as a Strongly Suggestive Symptom of Unilateral Tuberculosis."

Adjourned at 1 P.M.

FRIDAY, JUNE 1ST.

The President, Dr. Reginald H. Fitz, called the Association to order at 10.10 A.M.

The nominations for officers made by the Councillors and the nominations for membership approved by the Council were read by the Secretary.

Dr. V. C. Vaughan then read a paper entitled "The Chemical Products of the Anaërobic Putrefaction of Pancreatic and Hepatic Tissues and their Effects upon the Tests for Morphia."

Dr. H. M. Lyman read a paper entitled "Gastro-enteric Rheumatism," which was discussed by Drs. Musser, Graham, Vaughan, I. Dana, and Lyman.

Dr. George Dock read a paper entitled "A Case of Osteomalacia."

The paper of Dr. A. Jacobi, entitled "Stomatitis Neurotica;" that of Dr. A. McPhedran, entitled "A Case of Mitral Stenosis, with Great Hypertrophy of the Right Ventricle; Death from Hæmoptysis;" and that of Dr. J. H. Musser, entitled "A Case of Calculous Pyelitis, with Invasion by the Bacillus Lactis Aërogenes," were read by title.

On motion of Dr. Lyman, the Secretary was authorized to cast one ballot for the officers and nominees recommended by the Council, and the following officers and members were declared elected:

President.—Wm. Osler. *Vice-President.*—A. Jacobi.
Recorder.—I. Minis Hays. *Secretary.*—Henry Hun.
Treasurer.—W. W. Johnston. *Councillor.*—J. E. Graham.

Members.—Herman M. Biggs, of New York; Elbridge G. Cutler, of Boston; Francis H. Williams, of Boston; M. Howard Fussell, of Philadelphia; J. George Adami, of Montreal; B. K. Rachford, of Cincinnati.

Adjourned at 12 M.

HENRY HUN, *Secretary.*

NOTICE.

The Association assumes no responsibility for the statements and opinions expressed in the papers read at its meetings.

THE RISE AND FALL OF THE LICENSED PHYSICIAN IN MASSACHUSETTS, 1781–1860.

By REGINALD H. FITZ, M.D.,
OF BOSTON.

GENTLEMEN: In calling to order the Ninth Annual Meeting of our Association I desire to express the highest appreciation for the honor you have bestowed upon me in appointing me to preside over your proceedings. To conduct the affairs of so aristocratic a democracy has been made a task so easy that the gift of persuasion or the knowledge of parliamentary law become wholly unnecessary qualifications. The one obligation which has weighed somewhat heavily is the thought of the opening address which is to prepare the way for such communications as you are to make for the advancement of scientific and practical medicine—all the more as my own attention has been particularly directed for the past few months toward a class of practitioners who have no idea of scientific medicine, and whose only thought of the practice of medicine is how much money can be made out of it. It may not be uninteresting to learn what men like yourselves, many years ago, did in order to discourage such persons—what they planned, what they accomplished, and why they failed. I will, therefore, ask your attention to the rise and fall of licensed physicians in Massachusetts, 1781–1860.

In the "Records of the Governor and Company of the Massachusetts Bay in New England" (1854, III., 153) is to be found the first legislation concerning the regulation of medical practice in Massachusetts. On the 3d of May, 1649, the General Court, held at Boston, voted as follows:

"Forasmuch as the lawe of God (Exod: 20; 13) allowes no man to touch the life or limme of any pson except in a judicyall way, bee it hereby

ordered and decreed, that no pson or psons whatsoeuer that are imployed about the bodyes of men, woemen, and children for preservation of life or health, as phisitians, chirurgians, midwives, or others, shall presume to exercise or putt forth any act contrary to the knowne rules of arte, nor exercise any force, violence, or cruelty vpon or towards the bodyes of any, whether young or old,—no, not in the most difficult and desperate cases—wth out the advice and consent of such as are skilfull in the same arte, if such may be had, or at least of the wisest and gravest then present, and consent of the patient or patients (if they be mentis compotes), much lesse contrary to such advice and consent, vpon such punishment as the nature of the fact may deserve; w^{ch} law is not intended to discourage any from a lawfull vse of their skill, but rather to encourage and direct them in the right vse thereof, and to inhibit and restrayne the presumptuous arrogance of such as through præfidence of their ovne skill, or any other sinister respects, dare be bould to attempt to exercise any violence vpon or toward the bodies of young or old, to the prejudice or hazard of the life or limme of men, woemen, or children."

Until the years immediately preceding the War of the Revolution there was no more stringent regulation of medical practice than this. But in 1760 the city of New York had found it necessary to regulate the practice of medicine within its limits on account of the abundance of quacks preying upon the community. Five years later the Medical School of the University of Pennsylvania was established, and in the following year the New Jersey Medical Society was founded. In still another year the Medical School of Columbia College began its career; and in 1771 the colony of New Jersey passed its act regulating the practice of medicine, to be followed in 1774 by the abortive attempt in Connecticut.

The years thus ripe in revolutionary ideas and acts produced their fruit in Massachusetts.

Although there were excellent physicians in the larger cities and towns of the Commonwealth, and several of them possessed medical degrees received in Europe, they were few and far between. Most practitioners had served merely a sort of apprenticeship to their seniors. There was no medical school in the State, and but two in the country, and these almost as remote as the leading schools of Europe at the present day. Anyone undertook the study of medicine in such manner as he saw fit, and entered his practice with as little preparation as he chose. A considerable number of wholly unqualified practitioners thus were to be found, a source of danger

to the community, a disgrace to the name of physician, and a cause of jealously, contention, and distrust, among the members of the profession.[1]

The example set by New Jersey and New York was one which demanded a speedy following, and thirty-one of the leading physicians of Massachusetts, sixteen being from towns outside of Boston, became incorporated as the Massachusetts Medical Society, "that a just discrimination should be made between such as are duly educated, and properly qualified for the duties of their profession, and those who may ignorantly and wickedly administer medicine whereby the health and lives of many valuable individuals may be endangered, or perhaps lost to the community."

That this purpose might be carried out, the President and Fellows of the Society or their appointees from its members were given "full power and authority to examine all candidates for the practice of physic and surgery, who shall offer themselves for examination, respecting their skill in their profession, and if upon such examination the said candidates shall be found skilled in their profession, and fitted for the practice of it, they shall receive the approbation of the Society in letters testimonial of such examination," etc. They were obliged, under penalty, to hold this examination, although candidates were not obliged to present themselves for approval.

The State thus did not prevent the practice of medicine by anyone, but it implied that the letters testimonial of the Society discriminated between the duly educated and properly qualified, and the ignorant and wicked. By the limitation of the maximum membership to seventy, admission to the fellowship became a proof of distinction which the better educated and higher-minded physicians were proud to attain. This number, furthermore, gave evidence of the comparatively few physicians in the State at that time who were considered worthy of this high distinction. Indeed, it repeatedly happened in the early life of the Society that it was impossible to secure the attendance of a sufficient number of Fellows to form a quorum to transact business.

Two years after the incorporation of the Medical Society the Medical School of Harvard College was established; and it was

[1] Proceedings of the Massachusetts Medical Society, 1831, 19.

feared that the power of Harvard College to examine medical students and grant degrees in medicine might interfere with the authority of the Society to examine candidates for practice and issue letters testimonial. According to the memorial of Dr. John Warren in 1811, this "would have produced the most unhappy effects, but for the repeal of an exceptionable article in that establishment, and the accommodating conduct of those who, at that time, were the guardians of science and the patrons of the healing art."[1]

But doubts arose with reference to the duties and powers of the Society concerning the examination of candidates and its authority to demand and receive compensation for its services, and an act in addition to the act of incorporation was passed in 1789. It was therein made the duty of the Society, "in order more effectually to answer the designs of their institution, from time to time to describe and point out such a medical instruction, or education, as they shall judge requisite for candidates for the practice of physic and surgery, previous to their examination before them . . . . and they shall cause the same to be published in three newspapers in three different counties within this Commonwealth."

The Society continued to fail in its object to create a proper standard of medical qualifications. The population of the State rapidly increased, and the number of practitioners likewise. There was no sufficient inducement to lead physicians to apply for the approval of the Society; and in the first twenty years of its existence only some twenty candidates had received the testimonials in approval of their professional skill.[2] In the same period Harvard had conferred its medical degree upon thirty candidates.

Early in the present century Dr. John D. Treadwell, a young, learned, devoted and public-spirited physician of Salem, impressed with the inability of the Society to accomplish its aims, endeavored to improve its usefulness. An extensive correspondence was instituted among the members, and with the assistance of Mr. Sewell, afterward Chief Justice of the State, a bill was drafted, which, somewhat modified, was enacted in 1803.

The Massachusetts Medical Society, as it now exists, was then

[1] Dr. S. A. Green's Centennial Address, Med. Comm. Massachusetts Medical Society, 1875–81, xii 639, 654.

[2] Dr. James Jackson's Speech at the Annual Dinner, 1856.

instituted; and its plan of organization became a model for other State societies. It was no longer a close corporation with a limited membership, but it was possible for every physician in the State to become a Fellow. It was only necessary that he should have been a student in medicine agreeably to the regulations of the Society, and pass a satisfactory examination before the censors, after which he received a license to become a practitioner of medicine or surgery; "and after three years of approved practice in medicine and surgery, and being of good moral character, and not otherwise," he became a member of the corporation by subscribing to the by-laws.

The medical graduates of Harvard University were made licentiates without passing an examination, since the right to confer degrees had been granted Harvard College long before the Massachusetts Medical Society was incorporated. "The only means of avoiding collision with that ancient and respectable institution was by the compromise which was adopted." [1]

A duly licensed physician in Massachusetts in 1804 was required to give satisfactory evidence of the following qualifications before being admitted to examination for the license: Some acquaintance with Latin and Greek, and with the principles of geometry and natural philosophy; three full years of study under the direction of some respectable physician or physicians whose practice he must have attended. During this time he must have read the most approved authors in anatomy, physiology, chemistry, materia medica, surgery, and the theory and practice of physic. He was examined in physiology, pathology, therapeutics, and surgery.

There was still no obligation on the part of any practitioner to present himself for license; and the only privilege enjoyed by the licensed physician, apart from the right to attend the meetings of the Society and the use of its libraries, was exemption from service in the militia.

Notwithstanding the Act of 1803 made it possible for every properly qualified physician to become licensed and a member of the Society, it proved necessary to take further steps to bring them within the fold, and in 1806 a by-law was passed in the following terms:

[1] Proceedings Massachusetts Medical Society, 1881, 26.

"To promote the laudable design of the Legislature, in forming and incorporating this Society, to prevent as far as may be all unqualified persons from practising medicine or surgery, and in order to discourage empiricism and quackery: it shall be deemed disreputable and shall be unlawful, for any fellow of this Society, in the capacity of physician or surgeon to advise or consult with any person, who having been a fellow of the Society, shall be expelled therefrom, or with any person whatever, who shall thereafter commence the practice of medicine or surgery within this Commonwealth, until he shall have been duly examined and approbated by the censors of the Society or by those of some district society," etc.

The object of this by-law was to guard the public against ignorant, designing, and unscrupulous pretenders. The Society had provided the means by which physicians could give evidence of having followed a suitable course of study, and it was its duty to inform the public that if it employed unlicensed practitioners it must suffer the consequences.

Despite these attempts at compelling practitioners to become educated physicians, the standard was evidently too high for all to attain. Many could not comply with the requirements; others did not find a sufficient inducement in the honors and privileges bestowed by the Society. The Thomsonians, then beginning their career, required no education and no license. There was no law to prevent their entering practice; and Chief Justice Parsons[1] had then made his famous decision in the case of the Commonwealth *v.* Thomson, "that if the prisoner acted with an honest intention and expectation of curing the deceased by this treatment, although death, unexpected by him, was the consequence, he was not guilty of manslaughter. . . . . There is no law which prohibits any man from prescribing for a sick person with his consent if he honestly intends to cure him by his prescription; and it is not felony, if through his ignorance of the quality of the medicine prescribed or of the nature of the disease or of both, the patient, contrary to his expectation, should die."

The Chief Justice evidently felt that there was likely to be need of some legislation which should prevent the occurrence of such cases, for he closes his decision by saying:[2] "It is to be exceedingly lamented that people are so easily persuaded to put confidence in these itinerant quacks, and to trust their lives to strangers without

[1] Massachusetts Reports, 1809, vi. 134.

[2] Op. cit., p. 142.

knowledge or experience. If this astonishing infatuation should continue, and men are found to yield to the impudent pretensions of ignorant empiricism, there seems to be no adequate remedy by a criminal prosecution, without the interference of the legislature, if the quack, however weak and presumptuous, should prescribe with honest intentions and expectations of relieving his patients."

In 1811 an unsuccessful attempt was made to incorporate a rival society with the same privileges as those enjoyed by the Massachusetts Medical Society, under the title of the Massachusetts College of Physicians. The announced reason was that two societies were better than one; the real object was thought to be the establishment of a new medical school. The Massachusetts Medical Society strongly opposed the scheme, on the ground that it was unnecessary and would lead to the rejected candidates of the one society being accepted by the other, whatever might be their qualification, thus producing disagreements and animosities injurious to the profession and to the public.[1]

It is possible that in consequence of the recommendation of Chief Justice Parsons, certainly with the view of discouraging quackery, which was rapidly increasing under the influence of Thomson, the legislature in 1818 passed its first "Act regulating the Practice of Physick and Surgery," which was supplemented in 1819 by "an Act in addition to an Act entitled 'an Act regulating the Practice of Physick and Surgery.'"

According to the first of these Acts, no person entering the practice of physic and surgery within the State could recover by law any debt or fees for his professional services unless he had received a medical degree from some college or university, or had been duly licensed by some medical society or college of physicians, or by three Fellows of the Massachusetts Medical Society, designated in each county by its councillors, with power to examine candidates and grant licenses. Copies of these licenses were to be deposited with the clerk of the town, district, or plantation in which the licentiate resided.

In the Act of 1819, that the physician might recover his debts by law, it was necessary that he should be a licentiate of the Society

[1] Dr. S. A. Green, loc. cit., p. 651.

or a medical graduate of Harvard. If the candidate for the license was educated out of the State, the censors might waive a new examination if they were satisfied that he had received an education agreeably to the regulations provided by the Society.

It is stated[1] that this difficult trust was accepted with reluctance,[2] that the law was not sought for by the Society, and that it was doubtful whether its action was not rather injurious than beneficial. Of this law Chief Justice Shaw said :[3]

"It appears to us that the leading and sole purpose of this act was to guard the public against ignorance, negligence, and carelessness in the members of one of the most useful professions, and that the means were intended to be adapted to that object. If the power of licensing were given to the Medical Society exclusively, there would be much more plausible ground, at least, to maintain that the power was conferred on a body who would have a temptation to abuse it, so as to promote their private interests; but where the power is conferred equally on the university charged with the great interests both of general and professional education, and which cannot be perceived to have any such interest, that ground of argument seems to be wholly removed, and it seems difficult to perceive how a power which it is important to the community should be placed somewhere could be placed more safely. The courts are all of the opinion that the law in question is not repugnant to the Article of the Bill of Rights, above cited, and that its validity cannot be impeached on the ground that it is a violation of any principle of the constitution."

The licensing of physicians by the Society doubtless aided in restraining a certain number of practitioners from adopting some of the methods of the charlatan; but it did not interfere with the encouragement of the latter by the community. I am indebted to Dr. John Homans, 2d, for the opportunity of quoting from a letter of Dr. George C. Shattuck to Dr. Homans, written July 26, 1828. It gives evidence of the fondness for quackery in Boston at that time.

"The city has 60,000 (inhabitants?) and seventy-one regularly bred physicians. About one-half, from either youth or age, have not much to do. The irregular physicians are numerous, at the head of which, in popular influence, we may place Thomson, who has formed his botanical society, who have individually learned his system of practice by hot drops and sweating, etc. The disciples of this system, perhaps, may embrace one-

[1] Proceedings Massachusetts Medical Society, 1840, p. 68.
[2] Loc. cit., 1831, 10.
[3] Hewitt *v.* Charier, Jr., 16 Pick., 355.

sixth of the population of Boston. The patent medicines are employed in about, I believe, another sixth of the cases."

In 1831 the Society had reached such a degree of success in carrying out the objects of its incorporation that it included in its ranks "nearly every educated practitioner of medicine or surgery in the State.[1]

The line of distinction was so strongly drawn between its members and irregular practitioners "that the profession is no longer made responsible in the minds of men for the consequences of their ignorance and malpractice, nor its harmony disturbed by their misconduct; and they are much less successful than formerly in diverting the confidence of the community from regular physicians to themselves." [2]

At this time, however, there were certain discordant elements within the Society which threatened its prosperity and usefulness. Some of the younger physicians were dissatisfied with the clause in the act of 1803, which demanded a period of three years of probation in practice before admission to full membership in the Society. The legislature was therefore requested to repeal this clause, which it did by a special act in 1831, and approved candidates became at once Fellows of the Society.

A more serious disturbance, which menaced the harmony and influence of the Society at this time, was the appeal to the legislature from the physicians of Berkshire county, in the western part of the State. They desired to be incorporated as an independent body, nominally on account of their distance from the headquarters of the Society, their limited privileges, and their dissatisfaction with the requirements of the censors. It was supposed that this action was largely planned in the interests of the Berkshire Medical Institution, a medical school incorporated in 1823, but without the authority to confer the degree of Doctor of Medicine.[3] It was situated in Pittsfield, and was practically a department of Williams College (not far distant), which had the power to confer degrees, but no medical faculty or medical school. Williams College sanctioned the degree of the candidates educated at the Berkshire Medical Institution. The conditions of this alliance proved im-

[1] Proceedings Massachusetts Medical Society, 1831, 18.
[2] Loc. cit., 1831, 19.
[3] Loc. cit., 1836, 25.

portant in the courts[1] when the honorary degree of M.D. from Williams College was offered in evidence as a legal qualification. It was decided that it was invalid, since the defendant must have both the education and the degree to be a legally qualified practitioner.

In the year following the incorporation of the Berkshire Institution it had petitioned the legislature to be granted the same privileges as belonged to the medical graduates of Harvard University, the most important of which was that of being acknowledged and received by the Massachusetts Medical Society without examination as regular practitioners of medicine and surgery. At that time this petition was successfully opposed, on the ground that the Berkshire Institution had no independent board of overseers like Harvard College, and therefore was not under the same restrictions and oversight. The petition to form an independent society was also successfully opposed; but in 1837, with the approval of the Society, an act was passed, according to which graduates of the Berkshire Medical Institution were "entitled to all the rights, privileges, and immunities granted to the medical graduates of Harvard College."

The rights and privileges of the licentiates of the Massachusetts Medical Society had been somewhat extended by the Anatomical Law of 1834, according to which "the dead bodies of such persons as it may be required to bury at the public expense might be surrendered to any regular physician duly licensed according to the laws of this Commonwealth."

The State had thus definitely committed itself to the regulation of the practice of medicine by the acts of 1818 and 1819, and had placed the duty of licensing practitioners in the hands of the Massachusetts Medical Society. It conferred but few privileges on the licensed, namely, exemption from militia service and jury duty, the right to obtain and dissect the unclaimed bodies of those to be buried at the public expense, and to collect fees by law. But unlicensed physicians could take their pay in advance, and were not desirous of the privilege of consulting with the members of the Society. The Thomsonian movement was rapidly spreading throughout the country, appealing to the people by its simplicity

[1] Wright *v.* Lanckton, 19 Pick., 291.

and economy, its dogmatic assertions and reports of wonderful cures, its advocacy of vegetable remedies, and its cry of persecution.

The efforts of the Society to include within its ranks all educated practitioners, led in 1836 to the recognition of dentists as practitioners of medicine, since dental surgery was being studied and pursued scientifically by gentlemen of regular medical education.[1]

In the following year a further attempt was made in this direction by requiring that every licentiate or medical graduate of Harvard or Berkshire entitled to admission to the Society must enter within a year after being so entitled or be deemed an irregular practitioner. This term was applied to all practitioners in the State who were not fellows or licentiates of the Society, or doctors in medicine of Harvard or Berkshire. The above regulation was repealed three years later, since it took away "the freedom originally intended to be allowed to all regular physicians to join the Society or not, as they pleased," and stigmatized "as irregular practitioners gentlemen who have been recognized as competent physicians merely for the exercise of this freedom."[2]

In 1836, the Statutes of the Commonwealth were revised, and the report of the commissioners (1835, Part I., 125) includes all the legislation previously enacted, placing the control of the licensing of physicians in the power of the Society. But the Legislature did not accept the first section, which read as follows:

"No person who has commenced the practice of physic or surgery, since the year one thousand eight hundred and eighteen, or who shall hereafter commence the practice thereof, shall be entitled to maintain any action for the recovery of any debt or fee accruing for his professional services, unless he shall, previously to rendering these services, have been licensed by the officers of the Massachusetts Medical Society, as hereafter provided, or shall have been graduated a doctor in medicine in Harvard University, or in the Berkshire Medical Institution, by the authority of Williams College."

It also negatived a clause making the neglect to record a license a like disqualification to its non-possession. The Legislature approved this part of the report of the committee with the above exceptions, and it became Chapter 22 of the Revised Statues entitled "Regulations Concerning the Practice of Physic and Sur-

[1] Proceedings of the Massachusetts Medical Society, 1836, 116.

[2] Ibid., 1840, 72.

gery." According to Dr. J. Mason Warren,[1] the first section was omitted in accordance with the wishes of the greater part of the (State Medical) Society . . . as being in its action adverse to their interests. It served merely to excite sympathy, especially for the Thomsonians, and could not prevent them from receiving fees for services rendered.

The Society continued in its work of licensing physicians without apparent disturbance until 1848. At this time its effect in controlling the conditions of medical practice in the State is thus expressed by Dr. A. L. Peirson, of Salem, in behalf of a committee of which he was chairman:[2]

"We have steadily elevated our profession, by improving medical education, encouraging the harmony and honorable intercourse of its members, and have protected from the mischief of quackery, by discouraging every show of it among regular practitioners. This simple and efficient plan of the Society has accomplished all that was ever intended by its organization in 1803. . . . It is to be regretted that from natural causes, no way to be attributed to the form of organization, the concentrated action of the Society has not been equally felt in all parts of this extended Commonwealth."

According to Dr. Z. B. Adams,[3] there were at this time 1237 medical practitioners in Massachusetts, most of whom belonged to the Massachusetts Medical Society.

On the contrary, Dr. J. V. C. Smith presented the minority report of the same committee, in which he states:[4]

"The Society was once eminently useful in protecting the community from the encroachment of ignorant pretenders, . . . and it must be obvious to all that circumstances have greatly changed, our legislative tables have been completely turned, and will probably ever remain so. A license, or medical degree, is no longer requisite for the practice of medicine in Massachusetts, and no laws of the State, or of the Massachusetts Medical Society, are of any avail in guarding the entrance into the profession, or regulating the conduct of its members. . . . Less than one-half of the regular practitioners of medicine now nominally constitute the Society. In Berkshire, there are one hundred; less than twenty belong to the Society. In Hampden, one hundred and thirty (about); and of this number only

[1] Transactions of the Medical Society of the State of New York, 1844, 1845, 1846, vi. app. 40.
[2] Proceedings of the Massachusetts Medical Society, 1848, 142.
[3] Transactions of the American Medical Association, 1848, i. 366.
[4] Proceedings of the Massachusetts Medical Society, 1848, 150.

about twenty or twenty-five are members of the State Society. In some other counties there is doubtless a majority, while in others not one-half of the regular physicians are members. The number of Fellows of the Massachusetts Medical Society is not far from seven hundred, which is not probably one-half of the physicians in the State."

These reports were called forth by a resolution presented by Dr. Childs, of Pittsfield, involving a change in the organization of the Society for the purpose of advancing medical science, promoting harmony and good feeling in the profession, thereby contributing to the best interests of society.

Although the councillors largely favored the views expressed in the majority report, the existence of a considerable degree of dissatisfaction and the necessity of remedying it was apparent in the appointment of a committee to consider the question of altering the by-laws. This committee consisted of Drs. John Ware, A. L. Peirson, W. Lewis, J. Jeffries, J. V. C. Smith, H. H. Childs, and John C. Dalton. The report of this committee is especially valuable from the character of the latter and the recognition of the necessity of the Society to increase and consolidate its strength. They stated[1] that many members had often expressed the opinion that the society as constituted did not accomplish all of the purposes of which it was capable—and failed to secure the favor of the profession in remote parts of the State. Consequently only a limited number of physicians found it for their interest to become members. They were called upon to obey laws which they had no voice in making, and to contribute to the expenses of an organization in which they found it difficult to take part. The Society is but little known to those among whom they are thrown, thus has but little influence over them, and it is not necessary to their reputable standing among physicians nor to their success with the community that they should be connected with it.

The committee reported various amendments to the by-laws involving favorable action of the Legislature which took place in 1850. By-law V. permitted any reputable practitioner of medicine or surgery who had been in practice not less than fifteen years, to be admitted a Fellow, previously to 1852, by the District Society where he resides, by a vote of two-thirds of the members present at any stated meeting.

[1] Ibid., 155.

The Society was thus endeavoring to increase its influence in the one direction by licensing as many educated and intelligent physicians as possible, and even without examination in certain instances. This liberality, however, was to be controlled by what many now see to have been an unwise policy, namely, the treatment of the homœopathists.

In 1846,[1] an applicant for membership stated that he had great confidence in the efficacy of medicine "especially when prepared and prescribed agreeably to the directions of Hahneman." The councillors referred the application to the censors, with full powers to settle the matter, and they admitted the applicant to membership.

In the meantime the influence of homœopathy was increasing, and in 1850[2] it was moved "that all homœopathic practitioners are, or should be, denominated irregular practitioners, and, according to the By-Laws of this Society, made and provided, ought to be expelled from membership." This resolve was tabled on motion of Dr. Bigelow.

At the next meeting Drs. Hayward, O. W. Holmes, and J. B. S. Jackson were appointed a committee "to devise some course of action, to be pursued by the Society, in regard to all homœopathists." This committee reported as follows:[3]

"(1) *Resolved*, That any Fellow of this Society who makes application to resign his Fellowship in consequence of having adopted the principles and practice of homœopathy may be permitted to do so on paying his arrearages; but he shall not be entitled to any of the privileges of Fellowship, nor shall his name be retained in the List of Fellows.

"(2) *Resolved*, That a diploma from a homœopathic institution shall not be received as any evidence of a medical education; nor shall the Censors of the Society regard the attendance on the lectures of such institutions, nor the time passed at them, as qualifications which shall entitle candidates to an examination for a license from this Society."

This report was adopted. Three years later the question of homœopathy was again brought before the Society at the annual meeting.[4] The Essex North District Society there presented the following resolution:

"Forasmuch as there is no common ground of support or sympathy between homœopathy and allopathy;

[1] Loc. cit., 1846, 108.
[2] Proceedings Massachusetts Medical Society, 1850, 32.
[3] Loc. cit., 1850, 51.
[4] Loc. cit., 1853, 102.

"*Resolved*, That if the homœopaths are allowed to retain their regular standing in the Massachusetts Medical Society, and claim fellowship and counsel with allopaths, we, as consistent and conscientious individuals, request to be honorably discharged from our allegiance and connection with the parent Society."

Dr. Spofford presented the following resolution:

"That, while we recognize the right of regular physicians to use medicine in any quantity or doses which they may consider useful to their patients, we consider all use of the name of homœopathy in public papers, on signs or otherwise, as quackish and disreputable, and that all persons who make pretensions to homœopathic practice ought to be excluded from the Society."

These resolutions, together with the whole subject, were referred to the councillors, who appointed the following committee to report upon them: Drs. Bigelow, Metcalf, M. Wyman, Spofford, and Alden. Dr. Jacob Bigelow reported in February, 1854, and his report was laid on the table.

In the next year[1] the censors of the Suffolk District Society rejected a candidate for admission who avowed himself practising upon the principles styled homœopathy, on the ground that he was not "fitted for the practice of medicine." It was voted (February 7, 1855), on motion of Dr. Bowditch, "that the councillors approve of the course adopted by the censors of the Massachusetts Medical Society for Suffolk District."

In the following June this district society called the attention of the general society to defects in the By-laws concerning the expulsion of members, with reference to a remedy; and this question, together with that concerning the admission of members, was referred to a committee for a report. A few days later the latter reported. Their report was referred to the councillors for adoption. They, in turn, referred the report to a committee, which altered the recommendations; these were adopted by the councillors in February, 1856, and by the Society on May 29, 1856.

These alterations made it possible to expel a member for any breach of the By-laws, for which censure, expulsion, or deprivation of privilege was a penalty, and for any conduct unbecoming and unworthy an honorable physician and member of the Society, in addition to causes hitherto deemed sufficient. A carefully

[1] Loc. cit., 1855, 7.

arranged method of conducting trials for offences was also provided. The report of the committee of the councillors recommending these alterations stated that they had no definite measures to offer with regard to homœopathy, and submitted the subject to the judgment of the councillors. This part of the report was laid on the table without debate.[1]

June 3, 1856, four days after the adoption of the amended report by the Society, the Homœopathic Medical Society was incorporated by the Legislature. It was authorized to examine all candidates for membership, and, if qualified, give them the approbation of the Society. Its members were declared exempt from militia service.

In the following year the motion that all candidates for the Fellowship be examined by the censors was referred to a committee, reported upon favorably, and the Legislature passed a special act March 5, 1859, making this method the law.

At this time the revision of the statutes was again under consideration, and the Commissioners had made their report to the Legislature, in which the existing laws concerning the regulation of the practice of medicine were included. This report was referred to a joint committee, which was subdivided into special committees. The general committee referred the chapter concerning the regulation of medical practice to one of these special committees on May 16, 1859. It instructed this committee—

"by special order, to inquire into the expediency of omitting all that part of the chapter relating to the Massachusetts Medical Society and to the regulation of the practice of medicine; and on the 21st of May they reported to the general committee amendments striking out every section, and every line, and every word in that chapter which gave the Massachusetts Medical Society any power to examine or license physicians or surgeons, or to prescribe a course of study and qualifications for physicians or surgeons."[2]

Four days later the councillors appointed a committee consisting of Drs. J. Bigelow, A. A. Gould, J. Jeffries, G. C. Shattuck, H. J. Bigelow, H. H. Childs, and J. G. Metcalf, and "instructed them to look after the interests of the Society in the Legislature," and

[1] Loc. cit., 1856, 35.

[2] Argument of J. H. Benton, Jr., before the Committee on Public Health, 1885.

they were "authorized to take such measure to protect their interests as they may deem expedient."[1]

But, in the words of Mr. Benton—

"The general committee adopted these proposed amendments, with the addition of a change of title of the act from 'Regulations concerning the practice of physic and surgery' to 'of the promotion of anatomical science,' and that chapter now stands, with the same title as Chapter 81 of the Public Statutes. All the amendments were adopted by the Legislature, and were enacted December 28, 1859. . . . . The Legislature then deliberately took out of the law of the Commonwealth every provision for the regulation of the practice of medicine or surgery, or for the examination or qualification of physicians or surgeons."

The committee of the Society appointed to look after its interests in the Legislature recommended, October 5, 1859, that "no person shall hereafter be admitted a member of the Society who professes to cure diseases by spiritualism, homœopathy, or Thomsonianism," which was adopted. As evidence of the state of feeling at the time, it may be said that at the meeting at which this resolution was approved it was voted that the Society disclaim all responsibility for the sentiments contained in the annual address of the day previous. This had been delivered by Oliver Wendell Holmes, and was entitled "Currents and Counter-currents of Medical Science."

Thus we see that the Massachusetts Medical Society was organized in 1781 with the express purpose of making a just discrimination between duly educated and properly qualified practitioners and those who ignorantly and wickedly administer medicine. For many years its Fellows acted most judiciously in endeavoring to include within their number every educated and moral practitioner in the State. They accomplished this largely by the force of example, association, and united encouragement. The State made them the sole source of licenses to practise. The progress of Thomsonianism left their responsibilities essentially intact. The advent of homœopathy found them weak where they should have been strong—short-sighted where they should have been far-seeing. The leaders were obliged to follow, and the reproval of the censors prevailed against the wisdom of the councillors.

[1] Proceedings Massachusetts Medical Society, 1859, 112.

Homœopathic diplomas and homœopathic certificates are now accepted by the Society. Homœopathic physicians have been found fitted to practise by the great public, which decides this question for all. Ten years of increasing intolerance destroyed seventy years of enthusiastic effort, devoted labor, tactful management, and wise counsel in the public interest. The State revoked the control of medical practice, and the people have been the sufferers. The history of Massachusetts in this respect is the history of the country. She was one of the last of the States to lay down the control, and she will be one of the last to resume it.

Thanking you for the patience with which you have listened to an historical narrative which offers but little in the way of moral or example to our own Association, we will proceed to the business of the day.

THE TREATMENT OF CERTAIN SYMPTOMS OF CROUPOUS PNEUMONIA, PARTICULARLY IN ADULTS.

By BEVERLEY ROBINSON, M.D.,
OF NEW YORK.

The two symptoms in connection with the first stage of Croupous Pneumonia which are of special interest as regards the efficacy of treatment, are *pyrexia* and *pulmonary congestion.*

Personally, I have not thought it wise, as a rule, to give the modern antipyretic drugs except in occasional doses. Of these, I believe phenacetine to be the most satisfactory. It diminishes fever somewhat, and promotes sleep and the general comfort of the patient, without great risk of depression in a marked degree. Antifebrin in doses of two to three grains lowers temperature a degree or two, but without promoting the comfort of the patient or producing sleep. In doses of five grains or more, it is evidently depressing. Neither of these drugs should be given continuously, and as a rule, only when the temperature is over 103° Fahr. I rely very much more upon the use of spirits of Mindererus, citrate of potash, and sulphate of magnesia to reduce temperature by action on the different emunctories of the economy—skin, kidneys, and bowels—than I do upon the former remedies. I believe still that 3 to 5 grains of quinine every four to six hours, tends to diminish fever, while strengthening somewhat the heart, through diminution of local hyperæmia of the lungs, promotion of absorption of the fibrino-corpuscular exudation into the alveoli, and a possible antiseptic action on the blood itself.

As to the use of cold sponging, the ice coil, cold pack, or cool baths for the purpose of reducing temperature, I have come to the conclusion that they do not act in this manner with any special

efficacy, as they are usually employed. In this country, at least, treatment of croupous pneumonia with cold baths has not yet become frequent. Occasionally when the temperature passes beyond 104° Fahr. and is accompanied with delirium, rapid and feeble pulse, frequent respiration, and other evidences of intense poisoning, or adynamia, the tub bath at a temperature of 80° to 90° Fahr. may be usefully employed. Not that the temperature always falls much after the use of these baths, but combined with continuous frictions during the bath, they certainly quiet delirium, awaken latent nervous energy, and stimulate capillary circulation over the surface of the body.

While these effects are customary, according to those who have made frequent use of cold tubs in the treatment of croupous pneumonia, I must confess that until lately I have been very doubtful as to their beneficial action. More than once I have seen bad rather than good results follow immersion. The patient has become more cyanosed, dyspnœa more marked, and if anything, the pulmonary congestion more intense. I am inclined to believe that sponging is a decidedly wiser method than the tub baths in many cases, if it be combined, too, with friction to help improve the patient's condition through its combined action in lowering temperature slightly and in increasing nervous energy.

I am especially indebted to Dr. J. Nelson Teeter, House Physician of the Third Medical Division, Bellevue Hospital, N. Y., for the privilege of seeing several cases treated with cool bed baths. The results, by this means obtained in the wards of Drs. A. A. Smith and Herman N. Biggs, have been very satisfactory, and particularly so when compared, as I am informed, with the other modes of treatment employed at the same time and on the same class of patients. The advantages of the bed baths are the avoidance of moving and shock and the ease with which they can be given. The bed is simply covered with a rubber cloth extending well over the sides and foot of the bed. Underneath it and around the margin of the cloth, a rolled blanket is placed so as to form a sort of trough in which the patient lies while some water is poured into it and the sponging of the whole surface of the body conducted. The temperature of the water is lowered or raised, with ice or hot water, as may be desirable. The bath lasts from fifteen to thirty

minutes, and is repeated whenever the temperature exceeds 103° Fahr. The chilly sensations after the bath are moderate and easily subdued with stimulation and a hot-water bag to the feet. The patient expresses relief from the bath, his pulse becomes stronger and the nervous manifestations less pronounced. The temperature within an hour subsequent to the bath falls one or two degrees. No complications have occurred which could fairly be attributed to the bed tub bath. As there is no lifting or immersion of the entire body of the patient, one or two attendants can give these baths satisfactorily when required, and particularly among women, there is far less nervous dread of the bath than there is where an attempt is made to give the ordinary tub bath.

At St. Luke's Hospital I have had the opportunity to observe and carefully inquire into the use of aconitin, when given at this stage, and often at a later period, with respect to its action on the temperature and pulse. After many trials of this drug I have been led to believe that its use by itself may often be injurious by diminishing the energy of cardiac contractions, so that they are with some difficulty again strengthened. Even when combined in its use with digitalin, or digitalin and strychnine, it is not free at times from grave objections. Aconite, or aconitin, seems to act mainly by reducing the tension of the radial pulse, and lessening the number of heart beats, while it diminishes their strength by its paralyzing effect on the ganglia and nerves controlling cardiac contractions. This poisonous effect of aconite upon the heart through its motor ganglia may be shown by direct applications of the drug. As a result of these, the heart is slowed in a very threatening manner, and may stop in diastole.

According to the researches of Ringer and Murrell, aconite paralyzes all nitrogenous tissues, and it is in this way that the heart beats are retarded. Aconitin is an extremely virulent poison, and according to some authors, more powerful even than hydrocyanic acid. It is scarcely adapted to internal use, as even $\frac{1}{50}$ grain has produced alarming results.[1]

Patten states that the primary stimulation which aconite produces upon the vagus centre in the medulla slows the heart rate at first, but its depressant action upon the motor cardiac centres and

[1] Biddle's Materia Medica, 12th ed., pp. 236-237.

the vagus end-organs in the heart is soon manifested, and the heart rate becomes very rapid.[1] The primary stimulation of the heart is not only quickly effected, but is also produced by very small doses. If the drug be continued or given in large doses, the vasomotor centres become gradually paralyzed, the blood pressure falls greatly, and the pulse is exceedingly weak and irregular. Great muscular weakness and dyspnœa occur, the respiration being slow, shallow, and feeble. The dyspnœa, and probably the weakness also, depend to a considerable extent upon the feebleness of the circulation and consequent imperfect nutrition of the nervous centres.[2]

As regards its use in pneumonia, Phillips[3] states that within a few days he has noticed both reduction of temperature and pulse, and believes that it controls and removes the tendency to extension of the congestion. On the other hand, Dr. Wilson Fox did not find that it had any effect on the temperature. For my part, I do not believe that its action is desirable in the treatment of croupous pneumonia where the pulmonary congestion even of the other lung is often so considerable, and where we have to dread so frequently the gradual or rapid giving out of heart power. In this connection, I am glad to quote the following from Dr. Powell:

"We can frequently only conjecture the cause of the *pyrexia* in the early hours of pneumonia, and considering the nature and peculiar danger in the later stages of pneumonia, perhaps the worst treatment of this symptom is that very generally adopted, viz., the administration of aconite. The favorable issue of the disease usually turns upon the maintenance of heart power and vessel tonicity, both of which are lowered by aconite at the very outset, sometimes beyond recall, as has happened in cases that have come within my experience."

Of course, this evil effect of aconite is lessened or neutralized by simultaneous and frequent use of digitalin and strychnine; and yet I cannot believe, even with the neutralizing effect of these drugs, that aconite, in a disease of the type of croupous pneumonia, either "abates the symptoms or favors the removal of the products of inflammation by increasing elimination through the skin and kidneys;" or that "generally in fibrinous pneumonia aconite is sufficient up to the period of crisis."[4]

[1] Materia Medica, Potter, 4th ed., p. 77.
[2] Pharmacology, Therapeutics, and Materia Medica, Brunton, Philada., 1889, p. 833.
[3] Materia Medica, p. 7.
[4] Bartholow, Materia Medica, 8th ed., p. 673.

To my mind there are other drugs eminently more useful, not only theoretically but practically, and here I am speaking both of pulmonary congestion and of pyrexia, which is closely allied with it; and often, as it were, being increased in degree when the congestion is more extensive and intense.

I have never seen any drug act as well in this stage of pneumonia as small repeated doses of antimony. The salt I have given most frequently is not tartar emetic, but kermes mineral, or the oxysulphuret of antimony. I have given it in a mixture with syrup of gum and orange flower water, usually in doses of $\frac{1}{32}$ grain every two hours or every hour for a while; employed in this manner fever and pulmonary congestion diminish at times in a very obvious manner. Expectoration becomes easier and more abundant, and the sputa, from being very tenacious and viscid, are more fluid and brought up with relative ease and increased frequency. Thus the dyspnœa is lessened without doubt. Kermes mineral given in the way I have mentioned is not irritating to the digestive tract as tartar emetic often is, even in small doses. Moreover, it does not produce a collapsed condition. It can be given as an expectorant with particular advantage in pneumonias grafted upon bronchitis, which are so frequent among old people. It suits children also remarkably well, in whom the stomach often rebels against the use of tartar emetic.[1] To aid its advantageous effects, we should employ at times alcohol internally, and revulsives to the chest walls.

Kermes mineral was recommended formerly by Prof. Meigs as an invaluable medicine in childbed fevers to promote diaphoresis and to reduce the force of the circulation. We usually associate remorseless bleeding and the use of antimony (tartar emetic) with the name of Rasori (1837, Milan); and whenever this drug is referred to enthusiastically we are inclined to view it with some wholesome dread. Nevertheless, in pneumonia particularly, there is no doubt, in my mind, about the tolerance obtained for this drug, nor indeed of the possibility of its preventing or greatly modifying hepatization of lung tissue in some cases. Admitting that this statement should not be accepted as correct by some path-

[1] Dict. Encycloped. des Sci. Méd., 2 série, t. xxvi. p. 547.

ologists, yet such an expression of opinion would not change my own judgment of its utility.

As far back as 1841 Grisolle wrote that antimony improved the general condition in pneumonia, even though it might not change the local state and disposed the economy to receive other therapeutic agents. Certainly with such testimony and that of Trousseau (1831–1832), who says in speaking of the use of antimony in croupous pneumonia, "Nothing is more remarkable than the rapidity of recovery. There is no convalescence. Three days suffice sometimes to bring back the patient from the gate of the grave to a state of health;" we should avoid undue skepticism.

Sturges[1] takes the view that in the cases referred to by Trousseau the natural march of pneumonia was so much disguised by drug interference that wholly false conclusions were reached. I cannot admit this statement of Sturges as wholly correct, for while I have not seen such effects as those described by Trousseau from the action of antimony in pneumonia, neither have I ever seen what these words of Trousseau fairly describe, as Sturges states, "the natural course of the disease in many cases under our modern treatment." By this, I presume, he means expectancy; since otherwise natural course of disease appears to my mind a misnomer. In the tabular statement of the results of treatment of pneumonia by Grisolle we find in his third class where eighteen died out of thirty; "of the twelve who recovered, nine" in the greatest peril "improved rapidly under the antimony." (Sturges.) The patients improved under the antimony treatment with a rapidity unobserved in any other treatment, a statement corroborated, as we have seen, by Trousseau. (Sturges.) The probabilities are that the antimony (tartar emetic), which was given in doses of $\frac{1}{6}$ grain to 1 grain every hour or two, caused the frequent vomiting and stools from which patients thus treated suffered in the first twenty-four hours. "Nevertheless, in the concurrent testimony of two independent observers, the general improvement following these truly drastic measures was so obvious as to suggest the figure of a man snatched from the grave." (*Loc. cit.*, p. 395.)

I have become convinced that the great mistake made formerly

[1] Pneumonia, 2d ed., London, 1890.

was to employ the wrong salt and to use it in excessive doses. Against the kermes mineral employed in much smaller doses, frequently repeated, there are no such objections. And after the study of its action in a series of cases I am persuaded that this remedy is not futile, and is often of value in pneumonia as an expectorant, and in the other ways to which I have referred. Osler (p. 532) considers that it would be a real gain in cases of sthenic pneumonia "to loosen the cough and give to the sputa a certain degree of fluidity." Now, in my experience, these results are distinctly obtained with the rational use of kermes mineral in the first and second stages of croupous pneumonia.

Whenever the heart is particularly taxed by reason of the pulmonary congestion and a tendency to œdema, as shown by very numerous moist râles at the bases posteriorly, and more or less frothy expectoration combined with the sanguinolent or rusty sputa, I am confident that no drug produces the rapid and remarkable results of nitroglycerin given by the mouth, or better still, hypodermically. In these instances, we must not rigidly adhere to the ordinary dose of $\frac{1}{100}$ grain, but use $\frac{1}{50}$ or $\frac{1}{25}$, if the condition of the patient is imminently threatening. The tension of the pulse is by no means an invariable or true guide for the use of nitroglycerin under these circumstances, as frequently, when the pulse is very frequent, depressible and irregular, it will gain force by the use of this drug. Moreover, the cyanosis of lips, face, and upper surface of the body, together with the rapid, superficial, panting respiration, will both be favorably modified. The skin soon takes on a better color and the breathing becomes steadier, deeper, and slower.

The use of inhalations of oxygen in relieving pulmonary congestion has, in my experience, afforded marked temporary relief to breathing in the greater number of cases of pneumonia. There are, however, exceptions to this rule, and in a few instances not even relief was afforded, but the dyspnœa and subjective distress was, on the contrary, obviously increased by inhalations of this gas. The cases of general œdema were those, singular to relate, in which I have remarked the greatest extremes. While some patients thus affected were notably relieved, others were made more anxious, and if possible, still greater sufferers. I have not been able to

account invariably for these differences of action. I have assumed, however, that whenever the pulmonary engorgement was most considerable and yet independent apparently of right heart failure, the oxygen proved to be particularly serviceable. In instances in which the right heart finally gave way, and with increasing dyspnœa the accentuation of the second heart sound over the pulmonary orifice diminished notably in intensity, while the pulse remained small, feeble, frequent, and irregular, oxygen has not proven itself so important an agent for good; and yet some writers find "that when the condition is mainly one of cardiac failure and collapse, particular benefit is obtained. (*The Therapeutic Gazette*, March 15, 1894, p. 184.)

I shall be glad to have an expression of opinion on this point. Certainly there are cases of severe pneumonia in which the favorable action of oxygen is remarkable, and some of these are where cyanosis is most marked.

I am inclined to believe in the treatment of pneumonia, just as I am in the treatment of typhoid fever, that it is essential to have the patients drink abundantly of water, and not force them simply to take milk, beef-tea, or broths of different kinds, with the idea that all that is required is to give nutritious fluids and lose sight of the great importance of water given by the stomach to promote elimination of poisonous excreta through the skin and kidneys. Dr. Andrew H. Smith has insisted very forcibly, in my judgment, upon the importance of this indication in the following terms: "We are apt to give freely of albuminous substances, and too often the instinctive craving for simple water to dilute the blood and facilitate its passage through the lungs is met by the constant proffer of milk, beef-tea, etc., in which the water is spoiled for Nature's purpose by the addition of unnecessary food.[1] The abundant use of cold spring water, or it may be of soda or Apollinaris water, not only gives relief to the distressing thirst, but also helps reduce the fever and may diminish slightly the viscidity of the expectoration.[2] The drinking of the water in these cases is most useful, as it is in the treatment of typhoid fever, by promoting abundant diuresis. It thus favors as much as possible the elimination of the products of

[1] Amer. Journ. Med. Sci., Oct. 1890, and Tenth Internat. Med. Congress, Berlin.
[2] Osler, loc cit., p. 532.

organic disintegration. No doubt increased evaporation, or transpiration from the skin and lungs thus affected, reduces the abnormal temperature of the body.[1]

The proper use of alcohol in the treatment of pneumonia is one of the most difficult with which we have to do. Unquestionably in many instances it is very beneficial, and for different reasons. Putting aside its direct stimulating properties, it must be regarded as a very acceptable food in moderate amount. It is readily assimilable and easily oxidized. Moreover, it prevents tissue waste and diminishes the amount of carbon dioxide, thus helping respiration when this function is particularly embarrassed. Alcohol is a notable relaxor of vessels, and the capillary circulation is thus materially improved and relief afforded after this manner to a laboring heart and engorged vessels in the different internal viscera, lungs, liver, spleen, and kidneys.

Finally, alcohol gives nerve force, thus controlling adynamia, restlessness, wakefulness, delirium, particularly when all these symptoms are but the index of the intense general poisoning of the system in pneumonia. It seems, therefore, that it is generally judicious practice when any reasonable doubt prevails as to the condition of the patient with respect to any one of the numerous conditions which seem threatening to life, to give repeated and moderate doses of alcohol. I know of only two absolute counter-indications:

1. Cases in which the patient is already highly plethoric and where the mass of blood, rich apparently in all nutritive qualities, would merely have this state exaggerated, as it were, by alcohol which is so readily and rapidly assimilated, and thus becomes positively a hindrance to the vital function. (Smith.)

2. Cases in which the hepatic engorgement and gastric catarrh render the use of alcohol pernicious, because nausea and stomachal intolerance are increased by its exhibition even in moderate amount, and thus assimilation of food and water is prevented.

In these instances particularly we obtain great relief from repeated doses of calomel, small or moderate in amount, which arrest fermentative processes in the stomach and intestinal tract and decongest the portal circulation in the most evident manner. An

[1] Med. Record, July 4, 1891, p. 11.

engorged and sometimes tender liver, a hard and distended abdomen, are frequently dissipated by this medication. In this way notable relief is afforded both to the respiration and circulation, and not seldom the temperature will drop a degree or two after one or two free movements of the bowels. I am not at present referring to the use of calomel when the patient is first placed under treatment by the physician, but rather to cases in which treatment has continued for two or more days after the initial chill and where the tongue remains yellow and thickly coated with fur, while the breath is most offensive. Such an example was observed by me only a short time since, and I cannot urge too strongly the importance of watching and treating intelligently such conditions when they are clearly present.

The two dangers most to be feared in the stage of hepatization, as well as that of crisis, come undoubtedly from heart failure or pulmonary hyperæmia. The heart failure may come on suddenly, or manifest itself gradually. It may affect the entire heart, and in that case be, as a rule, caused by the intensity of the general poisoning of the system, or it may be occasioned by the giving way of the right heart under the dependence mainly of increasing pulmonary obstruction. This increased pulmonary obstruction is, moreover, evidently due in a measure not to the inflammatory nature of the disease, but rather to vascular paralysis, which comes on at any time from the fourth or fifth to the seventh or eighth day of the disease in numerous instances.

How are these conditions to be met? My own convictions are formally opposed to the use of digitalis, or digitalin, except in very small doses, and then only to control cardiac irregularity when it occurs. I have reached this opinion slowly. I feel confident, however, that it is based upon correct interpretation of pathological facts as they are offered to us. Digitalis, if it acts at all in any appreciable manner, must of necessity increase the power of the heart, at the same time that it narrows and closes up, so to speak, the circulation in small vessels. Now in instances in which passive congestion is already a great danger, this effect is precisely what we should most wish to avoid. Nor do I believe that this unfortunate effect can be properly prevented by the relaxing effects of aconite, or aconitin, on the peripheral circulation, particularly under the con-

ditions now referred to. It is true that I have never seen death ensue directly from the action of this drug at this time. I have known, however, the pulse to be lowered in a sudden and alarming manner, and it was necessary on more than one occasion to interrupt its use immediately, and to stimulate the patient freely according to every available method so as to restore failing strength to a semi-paralyzed heart, and even slight tension to the radial pulse.

Ever since Dr. Roosevelt[1] published his very striking communication on the hypodermic use of strychnine in large doses, I have watched the use of this drug in my treatment of pneumonia with increasing interest. I employ it habitually; at first by the mouth, and later, whenever there is evidence of heart failure coming on, either occasionally or frequently according to the hypodermic method. Sometimes in the latter instances, it is wise, and particularly when there is no marked stomachal intolerance, not to interrupt the use of strychnine by the mouth, but continue the use of the drug in this manner, and every two or three hours to give a hypodermic of strychnine from $\frac{1}{60}$ to $\frac{1}{30}$ grain. I have no doubt myself—and particularly in alcoholic subjects—that strychnine is a very useful drug. In others, the great objection to strychnine in too large or too frequent doses is to produce a condition of nervous irritability which is at times distressing and also interferes with any possibility of sleep, unless narcotics in injudicious doses are resorted to.

On several occasions already, when a patient's condition has seemed desperate, and after strychnine to the highest possible limit compatible with safety has been vainly employed, I have had at least temporary results of considerable value from the use of hypodermic injections of extract of coca, made up aseptically. I am of opinion, however, that we must rely also in these cases upon the use of nitroglycerin hypodermically in sufficient doses to restore the patient to a relatively good condition. These hypodermic injections, alternated with those of strychnine, will do what no other drugs in my experience will accomplish. The basis of the use of nitroglycerin is, as we all know, to bleed, so to speak, from the veins into the arteries, and thus allow the wearied and labor-

[1] New York Med. Record, Dec. 24, 1892, p. 728.

ing heart to have the opportunity to tide over a critical period, where saving its energy is of as much, if not more importance than our efforts to add to it.

In just such cases, bleeding was formerly employed with, as we know, at least the happiest temporary effects, and it is probable that except for this seemingly heroic measure many lives would have been inevitably lost. Bleeding was the only means in those days which would act efficiently and rapidly, and if relief were not thus afforded to the acute and grievously obstructed pulmonary circulation, the patient fell suddenly into collapse and died.[1] Let us not ignore the fact that these cases still occur and, in my judgment, must be treated still in this manner. Only one means will save them, and this means is bleeding. Such cases, in general, are those which are evidently sthenic in character and where the inflammatory lesion seems most marked from the beginning; those cases in which, after twenty-four or forty-eight hours, both lungs are so much congested from venous paralysis and insufficient heart-power, that drugs can have, do have, no visible good effect, unless we take away an abundant amount of blood by venesection. Of course, in such instances, if the patient is an alcoholic, we are greatly handicapped by reason of probable degeneration of heart, kidneys, and arteries; but we cannot be confident invariably to what extent this degeneration has gone, and we are frequently in the position of offering a man, practically, his last and only chance of survival.

Immediately after the blood-letting, we may be able to use nitroglycerin, strychnine, or caffeine, hypodermically, with the greatest benefit. Frequently, of course, we shall be grievously disappointed as to the result, and our patient will die speedily despite all our efforts to save him. Even though the kidneys are apparently in good condition and there is no albuminuria, these sudden fatal occurrences take place. In such instances at times temporary benefit results from venesection, and we hope and believe for a few hours that the patient's condition has been really helped. Soon, however, a change comes for the worse, and death may follow within a few hours.

In reflecting upon some of these cases in which I have at first

[1] Dict. Encyclopéd. des Sci. Méd., loc. cit., p. 297.

thought that the general pneumonic congestion was the direct, immediate cause of death, I have later concluded that a slowly forming ante-mortem heart-clot had much to do with the fatal termination. In one instance which I saw in consultation with Dr. I. E. Traub, of New York, and where we bled the patient about seventeen or eighteen ounces at the third day of the disease, we had at first notable relief to the breathing and circulation, but soon the symptoms of distress and restlessness came back in aggravated form, and the patient grew worse suddenly and died. In this case, no murmur could be heard in the cardiac region, and although the sounds were slightly muffled and the action extremely rapid, we only suspected the formation of heart-clot, without being able to affirm it. In view of the sudden death of the patient and without other sufficient causes satisfactorily to explain it, I now believe cardiac thrombosis was the immediate cause. I have not infrequently, especially in former years, and when I was a hospital interne, seen many autopsies where pneumonia undoubtedly occasioned the heart-clot which was the direct cause of death. While in these cases of pulmonary congestion I do not believe the venesection affords the relief which we should expect to derive from it, if this complication (heart-clot) had not arisen I am of opinion that if under these circumstances we should follow the venesection by the subcutaneous injection of a salt solution, we would possibly obtain happy results. It certainly seems rational to act in this manner, since we know that the chlorides in the first and second stages of pneumonia are passing too freely out of the blood, and no doubt require to be supplied. I am glad to note that another than myself has seen and utilized this indication with evident good effects. In a late number of the *Virginia Medical Monthly*, Dr. Cunningham, of Ensley, Alabama, contributes a very valuable paper, in which he writes that he employs hypodermoclysis of saline solution, daily, in just such cases, with the object of preventing cardiac failure, which he thinks may be due to ante-mortem clot.

In some cases, no doubt, it is mainly a toxæmia which weakens the heart, and not simply the mechanically increased resistance in the right chambers. This seems to be proven by the great fall in the pulse, as well as in the breathing, coincident with the crisis, although the physical signs over the affected lung-area may show

no appreciable changes. Under these circumstances, according to Shattuck, it is the maintenance of nerve force which we must try to secure. This means the avoidance of every unnecessary fatigue and the administration of the largest amount of the most nutritious liquid food which can be digested, with free ventilation of the apartment.[1]

The opinion above expressed is also in part shared by Balfour.[2] This author states that when the pneumonia has fairly begun, the two conditions which have been admitted hitherto to weaken the heart most are excessive consolidation of lung tissue and hyperpyrexia. As regards the former, he writes:

"Excessive exudation within the lung tissue impoverishes the blood, and must, therefore, act injuriously on a weak heart by enfeebling its tissue and starving its nerve centres; but as an obstacle to the circulation, throwing a strain upon the right heart, it is of small moment, as the instant the temperature falls convalescence proceeds uninterruptedly, the heart making no account of the apparent obstacle."

I would also say an emphatic word in favor of frequently repeated doses of *strong* black coffee. Black coffee and alcohol, particularly old brandy, or rum, by the stomach, will be assimilated and hold the vitality of the patient when other food or stimulant will be of little or no apparent benefit. And yet according to some writers, the notion that these liquors, viz., old brandy or whiskey, are to be preferred because of the "mellowing" properties conferred by age, should be condemned as a delusion. Such liquors are declared to be much more irritant to the stomach and less certain in their general supporting effects than pure ethyl alcohol deprived of aroma.[3]

We are told, indeed, that the best French cognac is, "with a few exceptions, nothing but the alcohol of beets, of poor molasses, changed and colored by the fabricator, by the addition of infusion of tea and various essences which give it bouquet." Such brandies are almost sure to contain methyl alcohol in quantity, certain when freely administered to do harm to the patient. Either such affirmations are false, or else I have been particularly fortunate in em-

[1] The Therapeutic Gazette, January 15, 1894, p. 42.
[2] Edinburgh Medical Journal, November, 1891.
[3] The Therapeutic Gazette, January 15, 1894. p. 36.

ploying cognac or whiskey which produced no such deleterious results.

In my judgment caffein does not replace the use of coffee, and for the reason that the caffeo-tannic acid in conjunction with certain extractive matter contained in coffee is probably nutritive, whereas in caffein we have only an alkaloid which increases the power of the cardiac contraction and raises somewhat arterial tension whilst promoting diuresis.

After Delafield (*American Text-book of the Theory and Practice of Medicine*, Pepper, vol. ii. 555), the treatment of the exudative inflammation which seems to him the most satisfactory, is that by the combined use of aconitin, digitalin, and whiskey. The aconitin ($\frac{1}{6}$ mgm.) and digitalin ($\frac{1}{8}$ mgm.) are given in tablet form together. The frequency with which they are repeated is regulated by the pulse. The endeavor is made to get a pulse about 80 and of good quality. This treatment requires careful watching and "if it be carried too far the pulse may fall to 30 and the patient pass into a condition approaching collapse."

According to some observers, it is mainly the action of aconite which slows the pulse, and it is this tablet which we should stop giving when the pulse reaches one hundred or loses notably its force and becomes irregular. According to others, it is the digitalin which reduces the frequency of the pulse, "while the aconite, acting upon the heat-producing as well as the vasomotor centre, brings down the temperature to about 100°. My own observation is to the effect that the aconitin has more power in reducing the pulse-rate than in lowering temperature. If, however, as is often the case, after giving the aconitin regularly every hour for twenty-four or thirty-six hours at the first, second, or third day of the disease, we are compelled to interrupt its use for awhile on account of general weakness or lowered arterial tension with irregular pulse, both pulse and temperature begin immediately to rise again and soon reach nearly their previous limit. It is very important to know, however, the provenance of these alkaloids, as I have frequently remarked that their action is seemingly variable, and at one time far more powerful than at another. If they are identical how is it that with Chonteaud's granules we can give $\frac{1}{2}$ mgr. or 1 mgr. every hour, and with Merck's the ordinary dose is $\frac{1}{6}$ or $\frac{1}{8}$

mgr., and the effects obtained from these different doses are apparently similar?

In the treatment followed at St. Luke's Hospital, New York, ½ mgr. doses of arseniate of strychnine are usually given together with the digitalin and aconitin. I have now had an opportunity of watching this treatment for a sufficient length of time to justify me in saying that I prefer the treatment as marked out by me in this paper to the one with the so-called "Trinity pill;" and I have come to this conclusion for the reasons given in what precedes. As near a perfect routine treatment for many cases of croupous pneumonia of moderate severity, as we now possess, seems to me to be found in the use of kermes mineral, strychnine, nitroglycerin, and alcohol in the manner described. Black coffee as food is much to be prized when other aliments, such as milk, or broths, only in very limited quantities can be taken or assimilated. Sponging the surface, cold affusions to the chest and limbs, the ice coil on the abdomen, bed baths with friction of the entire body, or tub baths with similar rubbings have been used by some, it is said, with great benefit for their combined tonic and antipyretic effect, but are still of uncertain efficacy for many. Venesection will occasionally save life when all other means fail, and where, without interfering in this manner death, will surely and rapidly follow.

Finally, we should advisedly conclude, as it seems to me, that so long as we shall not have discovered the specific agent capable of killing the microbe in the economy or at least rendering its development impossible by sterilizing the organic site, the treatment of pneumonia will remain a symptomatic one, varying according to the indications from simple expectoration up to the most active medication. (*Dict. Encyclopéd. des Sci. Méd.*, 2 sér., t. xxvi. p. 545.)

APPENDIX.

REPORT RECEIVED FROM DR. J. N. TEETER, HOUSE PHYSICIAN AT BELLEVUE HOSPITAL, NEW YORK.

The number of cases of acute lobar pneumonia treated in the Third Medical Division from October 1, 1893, until March 1, 1894, was 38; 11 of these died; 4 died within twelve hours after admission; 5 suffered from complications, as follows: 3 from delirium tremens, 1 from empyema and abscess of the liver, and 1 from acute diffuse nephritis.

Collectively the plan of treatment employed was, in brief, as follows:

Very few cases were received during the third stage, and simply opium was used for the pain. They usually came in during the second stage, and were then given a cathartic of calomel gr. v, sod. bicarb. gr. xv, with sal. Rochelle ℥ss given about eight hours later. The temperature, pulse, and respiration were taken six times during the twenty-four hours. If the temperature was 103° F. or over, a sponge bath with brisk friction was employed, the water being at a temperature of 50° F., and the whole bath continuing for thirty minutes. Temperature was usually reduced about 1° F., and the nervous disturbance, delirium, and restlessness were lessened, and sleep followed.

If the patient had been a drinker, *alcohol* was used in the form of whiskey, a ℥ss being given six times during twenty-four hours. In other cases this stimulant was withheld until called for by a weak and rapid pulse with diminished second sound of the heart. It was then given in ℥ss doses six times a day, or increased as necessary up to ℥ss doses every two hours. Opium was usually given throughout the course of the disease in the form of the plain tincture or McMunn's elixir, using iij to ♏v every four hours. This relieved pain and nervous disturbance.

Nitroglycerin was administered when called for by a pulse of high tension, or in cases where cyanosis occurred, indicating failure of the right ventricle. In some cases ♏iv of nitroglycerin, $\frac{1}{100}$ per cent. solution, every three hours was used with good effect.

Strychnia was given in all cases from the start, commencing with doses of gr. $\frac{1}{60}$ six times a day, and where cardiac weakness threatened it was increased up to gr. $\frac{1}{30}$ every three hours. It seemed to have a toning effect upon the heart's action, keeping the pulse regular and of good volume.

Digitalis was rarely used—only in a few cases where the pulse was very rapid (140–180) and feeble, and then it was always combined with glonoin.

In stage of convalescence, cod liver oil and tonics of iron, quinia, arsenic, and simple bitters were employed.

Report from Dr. D. Bovaird on Treatment of Pneumonia at Presbyterian Hospital.

Many cases, of course, require nothing more than confinement to bed, fluid diet, and careful nursing, and these things are routine for every pneumonia patient received. The fluid diet, as usual, consists mainly of milk and broths. Rarely the milk may require peptonizing on account of the condition of the stomach.

Temperature. Very often nothing is done directly for the temperature, as it does not seem to disturb the patient in any way. The temperature may run 104°, or even 105°, for some days, without giving the patient any apparent discomfort. In these cases we let it alone. On the other hand, where the patient feels the temperature, complains of the fever, is flushed, restless, and breathing rapidly from it, we resort to some antipyretic measures. A year ago the continuous bath at a temperature of 98° F. was employed in a number of cases, the results being satisfactory in part of the cases, in others not so. Dr. Hedges, who was directing the treatment at that time, was of the opinion that in the cases where there was a small area of consolidation, with high temperature and severe cerebral symptoms, the continuous bath did good; in the cases where the lung lesion was the larger factor and the symptoms of intoxication not so marked, the baths failed to benefit; whether or not they did harm it would be hard to say.

In the cases that were benefited, temperature, pulse, respiration, and mental condition all showed the favorable influence in about equal measure.

Instead of a continuous bath the routine administration of sponge baths with ice-cold water has been tried in quite a number of cases. (Bath being given, q. 4 h. if temp. was 103° or over.) For it we cannot say much. Usually it reduced the temperature and respiration; sometimes it did not. On the pulse the effect did not seem good. Usually the patients come out of such a bath shivering, more or less cyanotic, and very miserable, so that they dreaded them and pleaded to have them stopped. Oftentimes the distress caused by the anticipation and realization of the procedure were quite sufficient to neutralize any good effect which might have been obtained.

This year, so far as hydrotherapy is concerned, we have contented ourselves with the occasional administration of a sponge-bath with water at 65°. Such a bath continued for fifteen minutes, a patient who seems to be suffering from his fever usually enjoys and seems benefited by; but even such a bath we found was not desired very often during the course of the disease.

So far as drugs are concerned, we have rarely employed them for the reduction of the pneumonia temperature. Occasionally we have given a dose of phenacetin, or phenocoll—rarely antifebrine. In the doses employed we never saw any distinctly bad effects from them, but their effect on the temperature was variable, often failing to affect it to any extent.

The respiration. The rapidity of respiration being regularly dependent

on some other factor—the high temperature, feeble pulse, pleuritic pain, etc. —it was controlled by looking to the causative factor.

Pulse. To this symptom our attention was naturally most given. A rapid pulse (over 100), with a sharply accentuated second sound over the pulmonary valves, such as is regularly heard in pneumonia, was regarded as a plain indication for some stimulation. This was given by means of nitroglycerin, whiskey, and strychnine. The nitroglycerin would be begun in doses of gr. $\frac{1}{100}$ every two or three hours—sometimes by mouth, preferably by hypodermatic. Of whiskey we would give ℥ss every three or four hours to begin with. Strychnine was employed in doses of gr. $\frac{1}{30}$ to $\frac{1}{20}$ q. 4 h.

As the disease progressed and the strain on the heart became more severe, showing itself in greater rapidity, less strength, and more or less cyanosis, the quantity of each of these drugs would be increased, the nitroglycerin especially being pushed. We would first make the administration more frequent—every two hours, then every hour; then the quantity would be increased to gr. $\frac{1}{50}$ or even $\frac{1}{25}$; the rapidity of the pulse, the sharpness of the second sound (pulmonic), and the cyanosis being the points of indication. In most of the cases gr. $\frac{1}{100}$ q. 1 h. was quite sufficient to meet all the indications, but the most signal result I can recall was obtained in a case where the temperature was running about 105°, the pulse about 130, the respirations from 48 to 58, and the patient being extremely cyanotic. Here the nitroglycerin was pushed steadily till gr. $\frac{1}{25}$ was given q. 1 h. for some time, with a relief shown in pulse, respiration, and cyanosis, which was gratifying to the highest degree.

In the same way we pushed the whiskey to ℥ss to j q. 2 h. or q. 1 h., and the strychnine to as much as gr. $\frac{1}{20}$ q. 2 h. for a time. Of course, this heavy stimulation is not long continued, for the battle is usually soon decided one way or the other.

The good effects of this stimulation are commonly observed in a better color, easier respiration, and stronger pulse, although neither pulse nor respiration is slowed to any marked extent. With the improvement the second sound at the base usually becomes more natural (clear and not so sharp). Sometimes, of course, the sharpness of the sound disappears from progressing weakness of heart action, not from lessening of the peripheral tension and stronger heart action.

With the treatment outlined we do not often see the marked fall of respiration and pulse which are vaunted as the results attained by digitalin and aconitin, but we do see such relief in the severer symptoms as undoubtedly helps the patient to a final recovery.

Pain. For this symptom we sometimes strap the chest—a measure which certainly often affords immediate relief, and has the rational advantage that it gives rest to the inflamed part.

Often we employ counter-irritation by mustard or hot flaxseed poultices. Frequently we give morphine in moderate doses by mouth or hypodermatically, as the surest means of relieving pain and giving quiet rest.

Cough. We have practically never used expectorants. Ammonium chloride has been employed a few times, but without any definite results. When the cough was very troublesome morphine was resorted to, just as for the pain. Oftentimes the hot poultices seem to afford marked relief from cough as well as pain.

Cerebral symptoms. These were treated really in the same way as the temperature, the acute cerebral symptoms almost always accompanying the high temperature, and being relieved when the temperature was reduced.

For insomnia and restlessness we again often resort to morphine.

Report from Dr. D. McL. Barstow.

The treatment of pneumonia at the New York Hospital during the winters of 1892–93 and 1893–94 has been largely expectant. For the most part we have been content to treat the symptoms. Taking the more important of these in order, our treatment may be summed up briefly as follows:

Temperature. We have used the tubs to some extent, but without much benefit. We use them in cases with hyperpyrexia—a temperature showing a tendency to stay above 105° F., and reaching 107° F. at times. As these cases, however, regularly die, we have not been able to convince ourselves that the tubs did any good. The temperature sometimes drops a degree or more, but whether this is due to the baths or to the regular up-and-down course of pneumonia temperature, I am unable to express an opinion.

We sometimes use sponge-baths, but with a view rather to increasing the comfort of the patient than to reduce the temperature, which we have not found to come down under sponging more than a few tenths of a degree, and even this reduction is by no means constant.

In general, we do not regard a high temperature as a serious symptom, unless it be continuous. In the ordinary cases the temperature does not seem to influence the course of the disease.

Pulse. This we regard as the most important and reliable index of the patient's condition. Where it is rapid, unless it be too feeble, we take it every hour, and administer $\frac{1}{6}$ mgm. aconitin, if the pulse be above 100°. The aconitin has not seemed to us to have any very marked antipyretic action, but it slows the pulse and reduces the arterial tension, and seems to render the ordinary patient more comfortable. We have used the regular "Trinity pill," but we do not like it as well as to give the drugs separately, and withdraw one or another as the patient's condition seems to indicate.

Strychnine we have found very valuable in many cases. It acts as a cardiac stimulant, and is much safer than digitalis. In the bad cases, with œdema of the lungs, I have seen a patient do well under gr. $\frac{1}{30}$ by hypodermatic every hour, kept up for twenty-four hours. In these cases we watch for increased reflexes, muscular twitchings, etc., as an indication for stopping the drug.

Carbonate of ammonia, in the bad cases, we use a good deal as an adjunct to the strychnine. I have seen patients recover from very bad conditions

under its use in doses of gr. v every two hours, alternating with strychnine gr. $\frac{1}{30}$, both by hypodermatic. I have, however, seen hypodermatic abscesses occur from its too profuse administration.

A somewhat less extensive use of nitroglycerin has led us to believe that it is a very valuable drug in the cases of œdema of the lungs. Its cardiac stimulation, combined with its dilatation of the arterial system, thus bleeding the veins into the arteries and easing up the work of the right heart, give it a high place in our opinion.

Whiskey we have used very extensively. It seems to act as a food as well as a cardiac stimulant. It is perhaps most useful in the asthenic, poorly-nourished patients, and in the alcoholic cases, where we give it almost as a matter of routine, in the dose of from ℥iij to ℥viij by mouth in twenty-four hours.

Dyspnœa and cyanosis. The treatment of these conditions depends, of course, upon the cause, so far as it can be ascertained, in each case. If it be due to the pleuritic pains, we adopt strapping the chest, poultices, and small doses of morphine. If it be due to cardiac weakness, we use the above-mentioned drugs. If to the large extent of lungs involved, we employ oxygen inhalations, which have seemed to me very useful in these cases. If the dyspnœa be due to congestion and œdema of the lungs, we employ dry cups, cardiac stimulants, and ligation of the extremities, three being tied off at once, and each one remaining tied for twenty minutes. Personally I have not much confidence in this last measure, although in a few cases it has seemed to give benefit in combination with other measures.

Sleeplessness. Trional and morphine are our standbys in this condition. Trional in the ordinary cases, and morphine held in reserve. We never hesitate to give morphine unless the consolidation be *very extensive* in area, and even then we use it if necessary, and I have seen no bad effects from its use. Our usual dose is from $\frac{1}{6}$ to $\frac{1}{3}$ gr. hypodermatically. In the more violent alcoholic cases we have sometimes been forced to give hyoscine hydrobromate gr. $\frac{1}{100}$ by hypodermatic. This, however, we never give except as a last resort.

Complications. These are handled symptomatically, and always carefully watched for. In case of a failure to defervesce, we look first for pleuritic effusion, which we have found quite constant, especially in the form of empyema.

Report of Dr. Martin, House Physician St. Luke's Hospital, New York.

During the last few years the treatment most generally followed at St. Luke's Hospital, in the uncomplicated cases of lobar pneumonia seen early in the disease has been the administration of minute doses of aconitin, digitalin, and arseniate of strychnine.

The drugs are given in tablet form of digitalin mgm. $\frac{1}{8}$, of aconitine mgm. $\frac{1}{6}$, of arseniate of strychnine mgm. $\frac{1}{2}$ every hour. The pulse is

counted every hour, and whenever it is below 100 to the minute the aconitine is omitted. If the pulse is slow enough, but too feeble, whiskey is given at regular intervals.

By this method of treatment the pulse is usually made less frequent, and with the reduction of the pulse the patient is regularly made more comfortable, but neither the duration of the disease nor the mortality seems to have been altered.

The Report of the Treatment of Croupous Pneumonia at the Roosevelt Hospital, New York, by Dr. Charles Norris, House Physician, is omitted by request.—(B. R.)

DISCUSSION.

Dr. G. L. Peabody: I have listened, as we all have, to this very full summary of the symptomatic treatment of this disease. I think we are all in accord with Dr. Robinson that at the present time there is no possibility of any other treatment than the symptomatic treatment of pneumonia. It seems to me that he has covered most of the symptoms; but there is one symptom or combination of symptoms that I meet with which is a very distressing one, and one that it is important to treat, namely, pain together with insomnia. The insomnia is caused either by the pain or by an irritating and frequent cough, which is often quite out of proportion to the good which it does in promoting discharge of the exudation. As a matter of fact, I suppose the cough is of relatively little importance in promoting the discharge of the exudation. We all know there are many cases of croupous pneumonia which get well where the exudation is entirely absorbed; and probably in no case is any considerable proportion of it gotten rid of by expectoration.

It has happened to me a number of times, in following other doctors in hospital service, as we all have to do in New York, where the pernicious practice of short services in hospitals prevails, to find that my predecessors have fought shy of the administration of morphine in pneumonia. Frequently they have objected to the administration of morphine, even in minute doses in cough mixtures, on the ground that opium and its alkaloids impair the activity of the respiratory centre; and that, as the respiratory system is here at fault or impaired, it is undesirable to do anything that would still further impair it. I think that reasoning is very fallacious. It is not the respiratory centre that is impaired, it is the respiratory periphery, and small doses of morphine do not further impair the respiratory system of the thorax, but will often act as a cardiac stimulant, and aid matters in the chest. Small doses of morphine, given subcutaneously, will relieve the symptoms of pain or insomnia dependent upon pain or excessive cough, in a way that nothing else will. I would like to emphasize most

particularly my own personal experience in a very considerable number of cases, especially in hospital practice, of the efficacy of morphine subcutaneously, in doses of one-sixth of a grain repeated once or twice if necessary, during the course of the night, as a means of relieving pain and insomnia from excessive cough or pain.

I am a believer in the efficacy of cold water applied to the surface in hyperpyrexia. I do not think it is necessary to treat every case of pneumonia whose temperature reaches 103° by bed baths or any other form of baths; but if the temperature is particularly high or prostrating, then the bath is exceedingly valuable in conjunction with friction to the surface.

It seems to me that Dr. Robinson's experience as to the occurrence of heart-clot as a cause of death in pneumonia is so far at variance with my own that I do not like to omit saying a word about it. It has been my misfortune, or good fortune, perhaps, to make a large number of autopsies in cases of death from pneumonia, for in some of our epidemics of pneumonia in New York the mortality is very high. I have very rarely found heart-clot as a pathological condition in this or any other disease. It seems to me that the French authors particularly have been inclined to mistake a post-mortem for an ante-mortem heart-clot. They have relied for a differential diagnosis upon the imprint of the aortic valve upon the clot. They conclude that if the aortic valve be thoroughly impressed upon the clot, the clot must have been ante-mortem. This is fallacious. The heart-clot, while it does occur, is so infrequent that it is not possible to predict it or to avert it by treatment.

Dr. J. C. Wilson: I think we must all feel under obligations to Dr. Robinson for the very practical and suggestive way in which he has presented this subject. Croupous pneumonia is a disease of especial interest on account of its wide prevalence and on account of its high mortality. I think, however, that there are two or three points which have scarcely been emphasized sufficiently in the paper and which are of some practical importance. The first one relates to the extreme variations, the wide variability of the disease which we recognize as croupous pneumonia, both clinically and doubtless also pathologically. We have to deal with a pathological condition associated with certain clinical phenomena which vary within the widest limits, so that the croupous pneumonias of infancy, of early life, of adult life, and of old age, and the croupous pneumonias of alcoholic subjects, the croupous pneumonias which are secondary to antecedent infectious processes, the croupous pneumonias in which there are corresponding or equally varying local lesions, central pneumonias, apex pneumonias, crossed and double pneumonias and so on, give us a series of clinical pictures which present not only wide variations in symptoms but indicate an equally varying treatment; so that the treatment of pneumonia to-day, where we have no specific treatment to fall back upon, must be, in the first place, a treatment of expectancy; and in the second place a treatment in which the symptomatic factor must enter largely in the process. If we take the type

of pneumonia, the so-called sthenic pneumonia of early adult life, in individuals of previously good health, the expectant treatment, or nearly expectant, seems to give the most satisfactory result in hospital and private practice.

In reference to cold baths, our experience in the German Hospital in Philadelphia has not been satisfactory in the treatment of any form of pneumonia. The cases have not done well that have been immersed in the cold bath. In reference to the application of cold locally to the chest, at times it has seemed to be of decided benefit, although it is impossible to adduce statistics that are satisfactory in this respect. Nor, indeed, do I think either the clinical or the mortality statistics of pneumonia can ever be satisfactory unless very large collections of cases are taken in which groups of patients are regarded and provided for in the deductions from the statistics. I have repeatedly in the wards of the hospital, in cases of so-called sthenic pneumonia with high temperature and tendency to stupor, derived the greatest benefit from cold affusions, the patients being placed upon a protective cot, and water poured from a pitcher in quantities of a half gallon or gallon at a time over his head, face and neck and bare shoulders. I have seen a reaction from this treatment which has appeared in several instances to have been the turning point in the case and to have saved life.

In regard to venesection, it would appear from the literature, that too much attention is paid to the mechanical indications for this procedure. It seems to me that venesection in croupous pneumonia has often proved advantageous by relieving the toxæmia, by withdrawing from the blood in large volume the toxic principles to which the nervous symptoms and other serious symptoms must be due; so, therefore, I think very often venesection is useful where the old mechanical indications are not very well marked; and I find myself inclined more and more to the practice of venesection in suitable cases of pneumonia.

With reference to what Dr. Peabody has said about the use of opium, I am quite certain from my personal experience, that it is not only safe but often advantageous, in a large proportion of cases of pneumonia, to give small amounts of opium or morphia; and I have, unless there be distinct contra-indications aside from the volume of the exudate and its viscidity (which I do not regard as contra-indications at all), fallen into the habit of qualifying the expectancy of my treatment of pneumonia by the routine administration of small doses of Dover's powder, two, two-and-a-half or three grains, at intervals of two, three or four hours, according to the degree of pain or restlessness of patient, throughout the case. I was led to do this in the first place by the desire to relieve pain and agitation, and to induce some degree of somnolence in the patients. I have used it almost as a matter of routine because I have not only seen such symptoms relieved, but I have apparently seen the general course of the disease favorably influenced.

In regard to the intravenous or hypodermatic administration of large quan-

tities of sterilized salt solution, alluded to by Dr. Robinson, I would like to call the attention of the Association to the fact that this method has been practised to a considerable extent in the wards of the Philadelphia Hospital, by Dr. Henry, and in cases of this kind, with very satisfactory results, which have already been reported by that distinguished observer.

Dr. V. C. Vaughan: I do not propose to discuss the very interesting and able paper of Dr. Robinson. There is one point, however, which it would be unfortunate to allow to go unmentioned in this society. Evidently Dr. Robinson has used a so-called digitalin, the greater part of which is digitoxin, and not the true digitalin. The true digitalin, which has been studied by Pfaff, has a wholly different action from that described by Dr. Robinson.

Dr. B. Robinson: There was a purpose in this paper, and that purpose, perhaps, was not brought out sufficiently plain in my reading of it. My purpose is to oppose what seemingly is the conviction of a certain number of eminent practitioners in New York to-day, of the efficacy of the so-called "Trinity pill" or a modification thereof, in, I won't say curing pneumonia, but at least in modifying in a manifest way its threatening symptoms. I have observed this sufficiently to feel disposed, so far as I can, to contradict what is, as I believe, now the general practice of the Roosevelt Hospital, of the New York Hospital, a good deal of St. Luke's Hospital, and some of the Presbyterian Hospital. That was one of the purposes of this paper. Another purpose was to direct the attention to the fact that we are using drugs very often in a way that is not altogether rational, simply because we do not know what we are using. I went to Dr. Rice the other day and asked him what I was using. He gave me a lengthy and learned description, but when he was through I was not much the wiser. Dr. Delafield says that he uses, with the happiest effects, certain doses which certainly do not correspond with those employed in other hospitals with the same drugs. We find different doctors using what they suppose to be the same drug and securing different results and effects, which differences are due to the fact that the agents they employ are not the same.

Dr. J. W. Roosevelt: I wish to state that the "Trinity pill" is not used in all the cases at the Roosevelt Hospital. It has actually been used in about one-third of the cases during the last year.

A TREATMENT OF TYPHOID FEVER.

By SAMUEL A. FISK, A.M., M.D.,
OF DENVER, COLORADO.

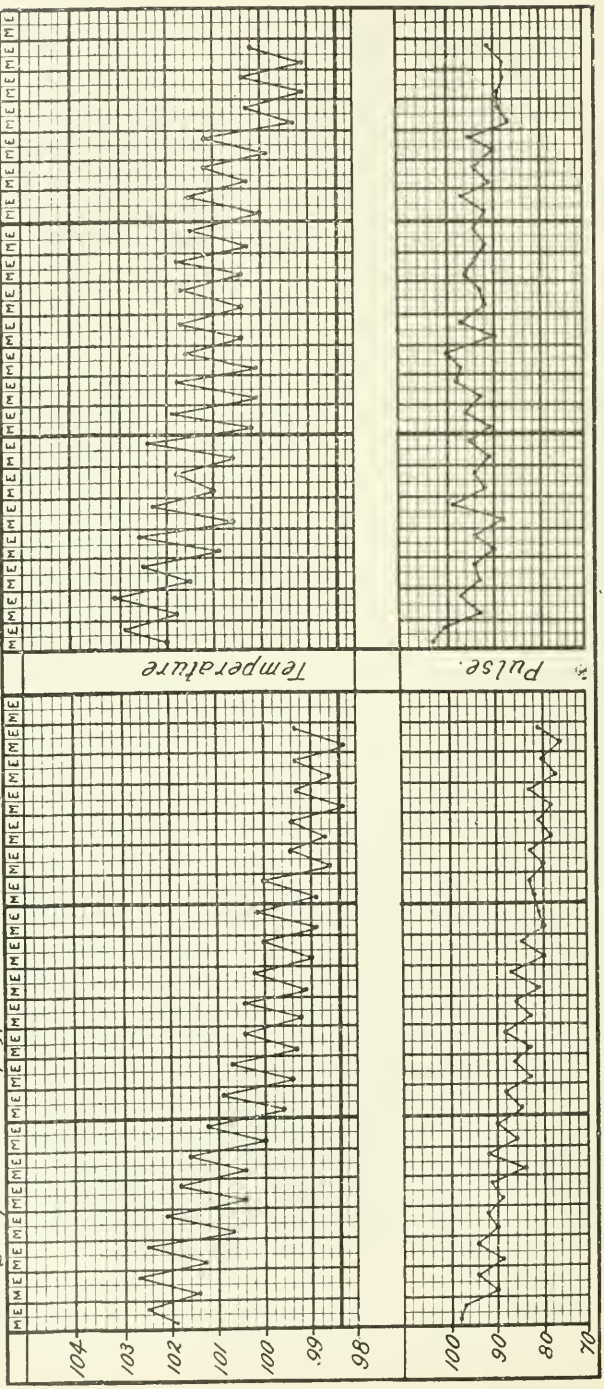
In these days when the Brand treatment of typhoid fever is the only one receiving any consideration, and the discussion, in medical circles, with reference to the treatment of this disease is confined to a consideration of hydrotherapy, it seems a little presumptuous for one to come forward with another presentation of the subject. My excuse must be that an observation of the results obtained by another method of procedure, extending over a number of years past, has led me to the conclusion that there is, in this method, something that is, at least, worthy of consideration. I am duly sensible that the presentation that I can give of my subject, at this time, is not based upon such a series of cases, so scientifically conducted, as to carry the fullest conviction, and my regret is that the hospital services of a somewhat new community do not afford the same opportunities for careful and scientific investigation as exist in older and more settled centres. That my opportunities for observation have not been altogether limited will be illustrated by a study of the mortality tables of Denver and of other cities.

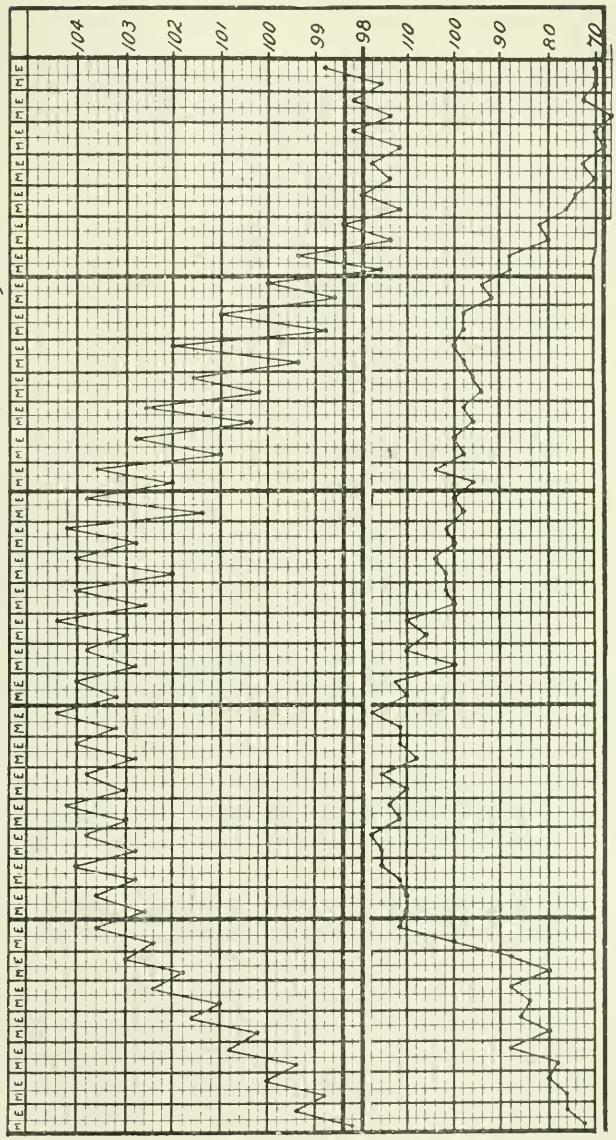
In his recent report on typhoid fever, Professor Osler states that for the years 1888 to 1892 inclusive Baltimore gives a yearly average of 229 fatal cases, Boston a yearly average of $160\frac{4}{10}$ fatal cases, New York a yearly average of $379\frac{4}{10}$ fatal cases, and Philadelphia a yearly average of $661\frac{8}{10}$, while Denver, for the same length of time, gives a yearly average of $149\frac{6}{10}$. My observation of typhoid fever, both in private practice and in hospital service, during these years has brought me to the belief that the line of treatment which I, in common with a few others in Denver, have followed was productive not only of a small rate of mortality—the exact ratio of

which I, unfortunately, cannot give—but also of a mild run of the fever, a minimum of complications, and a very decided diminution in the duration of the attack.

I beg to base my presentation of the subject on the accompanying charts. The first is a composite of thirty cases of typhoid, temperature and pulse, occurring under my own observation; the second is a composite of thirty cases, temperature and pulse, occurring in the services of other practitioners at the same hospital with myself, and I wish to state here that the composite is introduced with the consent of my confrères, and solely for the purpose of illustrating my subject. The third chart is taken from the article by Professor William Pepper, in his recent American text-book of *Theory and Practice of Medicine*, and is introduced as a typical chart of typhoid fever. The cases selected to make up the composite are assumed to be average cases scattered over three seasons, and are not taken with a view to influencing unduly the result. The composite in each case is obtained by adding the thirty morning temperatures on the day of admission and dividing by thirty, and so obtaining an average. The same is done with all the other morning and evening temperatures and pulse rates. For the accuracy and care with which this has been done I am indebted to my friend, Dr. C. D. Nelson, a recent graduate of the Harvard Medical School.

The composites seem to indicate that the average case in hospital service is obtained with us, as with Professor Osler, at about the end of the first week. A comparison of the composite of the thirty cases of my confrères, who did not use the Brand treatment, with the typical chart of Pepper, would seem to demonstrate that the average case of typhoid in Denver is a milder one than prevails in Eastern cities. But our mortality, averaging 1.50 deaths to every 1000 of population, shows that it is not without danger even here. Even allowing that the prevailing type is milder with us than elsewhere, which I am in doubts about, it nevertheless seems from the composite of my own thirty cases, as though treatment had a decided influence in affecting the type. So careful an observer as the late Dr. James H. Hutchinson has justly remarked that "Medicines are, however, by no means useless in the treatment of typhoid fever. There is no question that the disease is not only generally conducted to a favorable issue, but that its duration is


COMPARATIVE CHART
Average of 30 Cases of Typhoid Fever treated by Dr Fisk.
Average of 30 Cases of Typhoid Fever treated by Others.
Temperature
Pulse.
104
103
102
101
100
99
98
100
90
80
70


TYPICAL CHART OF TYPHOID FEVER (PEPPER)
104
103
102
101
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110
100
90
80
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M E

often materially shortened by their judicious use." My own composite would seem to illustrate the justice of this remark. I myself was greatly surprised to see the result of the composite. The steady decline of the temperature from the very start and a coincident decline of the pulse-rate are marked. It does not show the ordinary stage of *fastigium* with its two weeks' duration, and then the decline by *lysis*. It goes without saying, that with this decline in temperature and pulse is a steady improvement in all the symptoms. The patient, of course, loses flesh and strength. He is not apt to suffer from delirium, from tympanites, from dryness of the tongue, from sordes, or from tremor or any marked nervous symptoms. I might say that I never, or almost never, see a dry tongue, and such delirium as I witness is apt to be mild in character and confined to the night hours of the first few days, and generally disappears in a short time with the subsidence of the headache. In the main the treatment is as follows:

Absolute rest. If the patient is seen early in the attack, as gauged somewhat by the absence of rose spots and other constitutional symptoms, I give five grains of calomel at night, and follow it with a Seidlitz powder or some saline in the morning, and this is the only administration of calomel during the progress of the disease. I then put the patient on an absolute milk diet, giving a tumblerful every three hours. As a rule, I am not influenced by the patient's ideas that it is impossible to take milk, but determine that by my own observation. Where I find this to be true, I have the milk peptonized, and sometimes change to buttermilk. Extractive matters, in the way of broths and extracts, are not used, as they always seem to me to be harmful.

The turpentine mixture is becoming well known in our hospitals, and is meeting with great favor. It consists of:

℞.—Ol. terebenthinæ	. . . . .	ʒij.
Ol. ricini	. . . . .	ʒij.
Bismuthi subnitratis	. . . . .	ʒiv.
Mucil. acaciæ,	. . . . . q. s. ad	℥iv.

This must be shaken well, and a teaspoonful given in a little water twenty minutes after the goblet of milk. The turpentine in this seems to be sufficient to keep the tongue moist and to stimulate the

bowels; the castor-oil keeps up the secretions, and the bismuth acts, as is well known, as a dressing to the inflamed mucous surface; it also has a constipating effect, which is overcome by the administration of castor-oil, from a dessertspoonful to a tablespoonful every other morning. For the restlessness at night of the first few days, I use either five grains of Dover's powder, to be repeated once or twice during the night, or ten drops of McMunn's elixir of opium, to be repeated once or twice, if needed. Water, iced if preferred, is given freely, and lemonade, not too sweet, is allowed, not to conflict, however, with the taking of the milk. Antipyretics, like antipyrin, antifebrin, acetanilid, phenacetin, and even quinine (to reduce temperature), are absolutely forbidden. Stimulation, I reserve for necessity, as indicated by marked nervousness, a rapid and feeble pulse, and for the stage of convalescence. In both instances whiskey is preferred, care being taken to get a good quality. Of heart tonics, strophanthus is given preference. Strychnia is also used, especially in the stage of convalescence, and I frequently resort to hypodermatic administration of it in collapse and in profound prostration. The cold baths of Brand have never been resorted to by me, and, at the utmost, sponging with tepid water is sufficient, though not often employed.

I am convinced that great care must be taken in feeding a patient in the stage of convalescence. I think it is well to keep the patient on the milk diet indicated, increasing, however, the amount if needed, for a week after the temperature has come to the normal. I then begin to feed very gradually, preferring animal to starchy diet.

It will be seen that the methods employed are quite different from those advocated by others. The strict adherence to a milk diet, of course, is nothing new, and as far back as 1866 we find Dr. Cotting, of Roxbury, Massachusetts, reporting in the London *Lancet* 307 cases of typhoid treated without drugs of any kind and a mortality of only 10 per cent.

Professor Osler, in his recent publication, says: "Milk is the staple article of diet, of which from three to four pints are given in the twenty-four hours," which is about the amount that I have used. Dr. Hutchinson says: "Milk, as an article of diet, is unquestionably to be preferred to all others in typhoid fever."

The administration of turpentine was advocated by the late Professor George B. Wood, and indorsed by Dr. Hutchinson, though the dose employed was greatly in excess of that found in the turpentine mixture.

For the treatment as a whole, though not in every detail, I am indebted to my colleague, Dr. Edmund J. A. Rogers, of Denver, who, in common, with a few of the practitioners here, has used it with great success for a number of years.

In conclusion, my apology for the presentation of an article of this class must be found in the wording of Article I of the Constitution of this Association, which reads: "This Association has for its object the advance of scientific and practical medicine," and it is for the purpose of recording the results of practical observation rather than of scientific investigation that I have dared to detain you thus long.

DISCUSSION.

Dr. I. E. Atkinson: There are only two or three points that I wish to refer to, and my remarks upon them will be of rather a desultory character. I want to refer, first, to the use of milk in typhoid. I entirely agree with Dr. Fisk with regard to milk as the proper diet of typhoid fever patients, but I think it is a position that has to be taken with some qualifications. For example, toward the latter period of the typhoid fever cases, when the diarrhœa is brought under control, as we generally find to be the case, a considerable amount of difficulty often arises from the use of an exclusively milk diet in the tendency that the undigested portion of the casein of the milk has to accumulate in the rectum, and I have more than once satisfied myself that the fatal issue of a case of typhoid has begun with the labor-like pains the patient has had to expel this mass. I have a number times seen, and all of us have seen, this accumulation take place. I have a number of times been called in to see patients who had been completely exhausted by efforts of defecation, and I am certain that the strain upon the nervous system by such efforts has set up symptoms that have resulted in death. I, therefore, think that the judicious mingling of animal liquid food with the milk toward the end of treatment of typhoid fever is not only useful but desirable in nearly all cases.

The insomnia that the Doctor refers to is at times a matter of extreme importance, especially that insomnia which may be called the coma vigil, is extremely ominous, and I am satisfied that in a number of cases I have

averted fatal consequences by abandoning the use of ordinary hypnotics and using a slight inhalation of chloroform. I have known a number of cases in which the patient has been in a condition of insomnia for twenty-four to thirty-six hours or more, where the ordinary hypnotics have been given to the danger point, where a few whiffs of chloroform have allowed the patient to go into a slumber and permit the other hypnotics to assert themselves.

Regarding the amelioration of the general symptoms, I speak with a good deal of diffidence, because it is a matter that has been discussed over and over again. It has been well established that all the symptoms are favorably modified by the use of the cold bath. The dry, brown tongue is not present, there is absence of tympanites, of subsultus, of delirium and of profound depression, all due to the use of the cold bath, even where the temperature is only very temporarily modified. I have now a patient who is convalescing, having had seventy baths with a constantly recurring high temperature, 104° to 105° for two weeks, a condition which would have been followed by profound typhoid symptoms under ordinary methods, and in which the use of the cold bath prevented them all. The only bad symptom he had was elevated temperature.

The efficacy of the line of treatment which Dr. Fisk points out is not shown quite clearly by the chart. One or two cases widely different from the rule would have given quite a different picture. It is not shown that his method is as good as the cold-bath treatment now in vogue.

Dr. C. F. Folsom: A noted physician once reported seven years' experience with scarlet fever without death. He thought that he had found a specific. In the next two or three years he had so many more deaths than his colleagues had that his average was about the same as theirs. I cannot help thinking that Dr. Fisk has had the luck to have treated thirty unusually mild cases. I cannot think that his treatment had any material effect upon the progress of the disease.

Since I have been a visiting physician at the Boston City Hospital we have treated probably from 1500 to 2000 cases of typhoid. Of these I must have treated at least from 300 to 400. After I had treated 150 cases I was rash enough to write a paper and to generalize from my cases on the treatment of typhoid fever. Now, when I think that I need a little humiliation I refer to that paper. It seems to me that the reader's number of cases is altogether too small to generalize upon, and that, as Dr. Atkinson has said, our friend has not proved anything. In these 1500 to 2000 cases at the City Hospital, in addition to those of the previous twenty years, the whole range of treatment has been gone through with; there has been almost nothing suggested by our profession in the last twenty-five years that has not been tried, and I think that the pretty universal conclusion is that as a rule medicine, strictly speaking, has very little effect, except, in controlling symptoms which cannot be better controlled in other ways, and those are very few. Almost all the symptoms we find are best treated with

cold water. We have not got our mortality down as low as some of our colleagues think we ought to have it by 1 to 1½ deaths in 100; but we have a particularly hard class to deal with. It seems to me that our friend has not made his point.

Dr. J. F. A. Adams: I wish to say that it would be well if such charts as those of Dr. Fisk were more frequently made. It is a very good plan for us all to follow, and the more we have of such charts the better.

One thing that has struck me in this interesting paper is this, that typhoid fever in different parts of the country and at different times in the same locality is almost an entirely different disease.

In Western Massachusetts, about ten years ago, we had an invasion of intermittent fever, and following this invasion, typhoid fever became greatly changed, and I see in this chart an illustration of that very thing, and I wish to ask the question whether there is any intermittent fever in Denver.

Dr. Fisk: No, sir; not originating there. If a patient has contracted it elsewhere it is apt to crop out.

Dr. Adams: The type of typhoid fever, after malaria had appeared and disappeared, instead of following the typical chart of Dr. Pepper, followed more nearly this Denver chart. It began in the first week with a very high temperature and with chills. The highest temperature was in the first week, and then it rapidly subsided, running its course in two or three weeks, being a much more severe disease at the outset, but very seldom fatal, as if in some way its type had been changed by the presence of malaria. The mortality was very much diminished, and every treatment that was used during the two or three years following the invasion of malaria was highly successful; and every physician congratulated himself that he had found a remedy for typhoid fever. We found, however, on comparing notes that we were all using different remedies and all were very successful, because of the mild and short form of typhoid fever.

Dr. Wm. Osler: This paper is of considerable interest as illustrating a common therapeutic fallacy, since it must be doubtful whether Dr. Fisk's treatment had any influence on the disease. The chart indicates that he had a peculiarly mild series of cases, which would have, I am convinced (and I think that Dr. Fisk will ultimately agree with me), recovered with diet and a nurse.

I would like to mention that for the year ending May 15th there have been treated eighty cases in my wards (by the Brand method) with a mortality of only just over 6 per cent., which is a very satisfactory showing for a general hospital to which the cases are brought in at all stages.

Dr. Fisk: I will only say in reply that the criticisms which have been made are nothing more than I expected. I hope that sometime you gentle-

men will be in Denver in the typhoid season, and that I may have the pleasure of taking you around the hospital wards and showing you what we call typhoid fever and the results of this treatment. That it is a specific, I will not say, but it is something that we have employed satisfactorily in Denver for many years, and we have had considerable typhoid fever.

In the fall of 1890 we had 700 cases during the month of October. We have our epidemics of it in Denver as elsewhere. We may not have as severe a type as in the East, but we have what we call typhoid fever, even though we may all be ignoramuses and know nothing about it. My thirty cases are not by any means all that I have treated. Unfortunately, I have not been able to secure records, as can be done in Eastern hospitals. It seems to me that there are other ways of treating typhoid fever than by cold baths.

CASES OF TRAUMATIC HEADACHE.

By CHARLES F. FOLSOM, M.D.,
OF BOSTON, MASS.

In studying the various causes of headache, I have grouped together six similar cases due to traumatism which I report to-day. Others, where the injury was to the nose, are not included, inasmuch as the cause of the symptoms in them was complex.

Case I.—C. H., aged seventeen years, with healthy antecedents, strong, well developed and nourished, and sensibly brought up, was referred to me in October, 1890, by Dr. Hasket Derby, who had carefully examined his eyes and found them without defect. Four years previous to my seeing him, he was thrown from a horse and struck by the freshly-shod hoof of another horse, over the upper and middle region of the left parietal bone. There was a large irregular cut in the scalp which bled freely and finally healed by granulation. There was no unconsciousness after the accident and there were no cerebral symptoms at that time.

A year later, he began to have headache now and then, which was not severe, but which, still a year later, had become very bad and more frequent. These headaches began just back of the left eye, a couple of inches anterior to the cicatrix, extended over the temporal region, and finally involved the whole head. They lasted several days and were quite disabling. They were not affected in a causative way by the use of the eyes. The headaches became more and more troublesome until the summer of 1890, when they were almost constant, although the boy was at the time leading an outdoor life on a farm where he was passing his vacation. He made as little as possible of his symptoms, as he was very desirous of returning to school, which he did in October. He was not able to study and was sent back to me by his teacher as being in constant suffering. From his mother, whom I then saw for the first time, I learned that he had been obliged to give up the active occupations and amusements of boyhood, and walked about, and especially up and down stairs, with the greatest care in order to avoid the least jar, which made his head much worse. He could not study or read and there was no let-up to the pain which varied from time to time in degrees of severity. There had never been any convulsions or vomiting.

Physical examination of the patient was negative, except that over the upper middle part of the left parietal bone there was an irregular cicatrix, quite tender on pressure, about an inch and a quarter long, and three-sixteenths of an inch wide at the widest part. The boy had the general appearance of health, except that his face usually had the expression of pain. He was unnaturally irritable, and disagreeable to himself and to others.

After four years of medical treatment, it did not seem wise to try that any further. I advised that the cicatricial tissue should be cut out and that trephining or further exploration should depend upon the indications—an opinion in which Dr. Weir Mitchell concurred after seeing the patient in consultation.

The operation was performed by Dr. Warren, October 29th, in the presence of Dr. Weir Mitchell, Dr. C. B. Porter, and myself, but nothing was found to justify any apprehension of possible serious injury to the brain. There were three small indentations in the external table of the skull and trephining showed some reddening of the dura with adhesions to the adjacent bone. Dr. W. F. Whitney found, on microscopical examination, diffuse hyperostosis of the skull and interstitial neuritis in the cicatrized tissue.

The patient made a complete recovery, has been able to resume his studies, and has remained entirely well.

Case II.—Miss ——, aged twenty years, was seen by me in January, 1891, complaining of persistent dull headache, obstinate constipation which did not yield to ordinary remedies, and of paroxysms of severe pain throughout the head, with mental confusion beginning a few days before menstruation and lasting a week or more.

The patient's health had otherwise been excellent except for debility and some neurasthenic symptoms of three years' duration, which began a few months before the appearance of her headaches, and which had been attributed in part to worry and in part to a life involving some exposure on a cattle ranch in the West, with food not altogether suited to her somewhat exacting needs. She had lost twenty pounds in weight.

The family history was negative.

In July, 1884, the patient was kicked in the head over the upper and posterior portion of the right temporal bone by a well-shod horse. There was a large irregular scalp wound which got filled with sand and gravel. The wound was tied up and healed by granulation. There had been no unconsciousness or cerebral symptoms of any kind. There was no headache of consequence until nearly four years later, in 1888, when she was again thrown from a horse and dragged about fifty feet, being debilitated at the time. She was also generally bruised about the same time in a third accident with a horse. Then severe and persistent headaches began, gradually becoming worse, and being at last completely disabling a few days before menstruation.

The more or less constant headache was quite moderate in degree and attended with slight mental confusion, which became quite marked at the time of the severe headaches of the menstrual period. There was also a

degree of a peculiar motor aphasia at such times with hysterical symptoms, and there were often acts of cerebral automatism and attacks resembling petit mal.

After fourteen months of treatment the general health was restored, the constipation was relieved, and the persistent headache was somewhat better, but the paroxysmal attacks which have been described were not very much improved. There was nothing peculiar in the character of the headaches, which were general all over the head; and there was no tenderness in or near the cicatrix, which was irregular and ragged in shape, an inch and three-quarters long, and at the widest part nearly a quarter of an inch broad. It may be said in passing, that in this case and in the preceding case, the diagnosis had been made of *contrecoup* injury to the brain.

The cicatrix was removed by Dr. Warren in March, 1892, with complete relief to all the symptoms which I have enumerated.

Dr. W. F. Whitney found in the cicatricial tissue marked interstitial neuritis.

Case III.—F. R., aged eleven years, seen November, 1892, in consultation with Dr. V. Y. Bowditch; of neurotic temperament and family history.

In 1886 he was stunned by a fall, striking on a curbstone, with the result of a small scalp wound over the right frontal region about an inch above the supra-orbital ridge. In 1888 he was thrown from a small cart over a stone fence and was unconscious for a considerable time. There was a small scalp wound over the superior and posterior portion of the right temporal bone from this accident. In the same year he was partially stunned by being thrown from the rear platform of a street-car. His only serious illness had been intermittent fever in Italy.

Between two and three years after the second injury to the head he began to have persistent headache of slight degree, with frequent paroxysms of intense pain throughout the head. He lost flesh, became very thin and irritable, and had to give up study and reading. He also had frequent attacks of partial loss of consciousness, the precise nature of which I never ascertained. The only one which I saw resembled petit mal, and probably was that. The eyes had been examined by an expert and found without defect. Medical treatment had been exhausted.

The two small, faint cicatrices were excised by Dr. Warren, November 23, 1892. The relief from the operation was not immediate, but gradual, and in a month's time the patient was virtually well in every respect. Two months later he was run over by a sled, the runner striking the upper cicatrix, and he was at about the same time accidentally struck a heavy blow over the other scar. There were pain and tenderness over both for three days, and the headaches returned, to be soon relieved by massage, and the patient returned to his school. A short time afterward a new type of headaches appeared which were distinctly periodic and in part yielded to quinine, but which did not absolutely disappear until a re-examination of the eyes and the use of glasses for a trifling astigmatism.

Interstitial neuritis was found in the tissue of one scar by Dr. W. F.

Whitney. There was considerable cell infiltration around the perineurium, as in the other cases.

These three cases were reported chiefly from the pathological point of view, and with illustrations of sections under the microscope, by Dr. Warren at last year's meeting of the American Surgical Association.

Case IV.—Miss ——, aged nineteen years, seen by me in February, 1891. Family history good, except for recent alcoholism in one of the parents.

At the age of eleven years she struck her head violently against a spike, making a wound through the scalp which left an irregular, ragged cicatrix an inch long just to the right of the median line, and over the posterior portion of the parietal bone. Six years later the patient fell backward from a piazza eight feet high, striking the back of her head on a rock. She was unconscious for some time, and for several months there were pain and tenderness at the seat of the injury. There was no flesh wound.

Very troublesome headaches appeared a few years after the first injury, and were not increased after the second accident. They did not yield to treatment, and were so constant and severe that the patient had to give up school, and finally all mental work. The disability increased, and there had been for a year before I saw her, a dull mental state, occasional mild melancholia, cataleptiform attacks, and imperative conceptions, with a generally debilitated physical condition.

The patient was well developed; not well nourished; the internal organs and the eyes were free from disease or defect.

After trying medical treatment for four months without much benefit, except to make the physical state one of apparent health, I advised excision of the cicatricial tissue, which was done by Dr. Post, June, 1891. The result was entirely satisfactory in dispelling the headaches and all the morbid nervous and mental symptoms.

Case V.—W. ——, aged thirteen years, was first seen by me in 1884. There was a neurotic tendency in the family, which his parents had tried to counteract by country life and sensible habits of living. The boy was physically strong, well formed, and with the external appearance of physical health.

Somewhere about 1880 to 1882, he had received three severe blows on the head, the precise dates of which could not be learned, in play with other boys. From two there was no indication as to the site of the injury. The third, from the corner edge of a hoe, left a ragged scar a little over an inch long over the upper and superior portion of the right parietal bone. I could not ascertain just when his headaches appeared, as the precise time had been forgotten; but it was some months after the injuries, and when I saw the patient they had become entirely disabling, so that the boy was obliged to give up the common occupations and amusements of his age. He was irri-

table to the last degree, with very little initiative, or interest, or power of self-control, timid and apprehensive. He had frequent attacks of loss of consciousness, no one of which I ever saw, but which I supposed to be petit mal. A description of his various nervous and mental morbid symptoms, including a very curious type of topophobia, for the next six years, occupy many pages of my note-books.

Treatment for seven years under the most favorable conditions, the greater part of which was in the country under judicious direction, and away from home, was only disappointing in its results. Although there was some gain, the patient was a young man of twenty years quite unable to take his part in the world in anything but the simplest vegetative life.

The cicatrized tissue was excised by Dr. Post, June, 1891. The headaches ceased at once, and all the other neurasthenic and mental symptoms almost as soon. The young man entered a large business house, in which he worked hard and has done well.

Case VI.—Miss ——, seen in 1882, on account of frequent and severe epileptic convulsions. She was nineteen years of age, well developed, talented, accomplished, with a well-trained mind.

The family history was excellent.

Ten years before, when she was nine years old, she fell backward from a high swing and struck the back of her head violently on the ground. A few weeks later she began to have attacks of petit mal, which, as time went on, became more frequent, and in a few years there were also typical epileptic seizures, which occurred mostly at night or before breakfast in the morning. She had been under the care of the leading specialists in Boston and New York, and had been treated by Dr. Brown-Séquard. None of the treatment did any good, and some made her worse. After exhausting, as she supposed, the regular Pharmacopœia, she was taking a proprietary medicine which, on chemical examination, proved to be chiefly bromides; and while fully bromidized, she had more severe and more frequent attacks of epilepsy than ever before.

She had had for many years—none of the family could say how many—a persistent nagging headache, which had at last made her excessively irritable and difficult to get on with, although she was naturally most amiable.

Nothing abnormal was detected on physical examination. To bodily symmetry there was added a highly-trained, well-developed mind. No cicatrix was found, only a slight local tenderness on hard pressure.

The attacks of petit mal were often from twenty to thirty in twenty-four hours, and the grand mal once in a few weeks. After nine years of treatment the patient was, to all appearances, in a condition of blooming physical health. Very few people knew of her frequent attacks of petit mal, which were mostly in the morning, and of true epilepsy once in two to four months. The headache, chiefly in the back part of the head, persisted and the patient had become more irritable and self-willed, more difficult to live with, in spite of greatly improved general health.

This patient, by the way, is the only one in my experience who has taken

borax for a long period of years with greater benefit than from any other medicine.

The sensitive area, about as large as a silver half-dollar, remained just to the right of the median line and above the occipital protuberance where she struck when she fell, and where a marked unevenness could be felt on the outside of the skull.

It was thought that the conditions might be similar to what was found in the first case reported, and such proved to be the fact. The operation of trephining was done by Dr. Bradford, assisted by Dr. Monks and Dr. Brackett, in September, 1891. There was no distinct indication for opening the dura, and that was not done. The bone removed was quite irregular in thickness, but was, unfortunately, lost on the way to the pathologist.

As a result of the operation, the headaches quite disappeared, the attacks of both kinds have greatly diminished in frequency, and the irritability and impaired self-control are things of the past. The young lady's parents say that life with her is now a constant pleasure, and she herself takes her full part in social life, believing that, as she rather over-states the results, she has had a new life given her.

Observations might be made, and inferences could be drawn, and pathological theories and physiological speculations are possible, on these cases, that would be interesting and perhaps instructive. But I have not had time to make them short, and you have not the time for me to make them long.

The symptoms described were evidently reflex and secondary for the most part. So far as they were direct, they were due to more or less extensive alterations in the nerve and to the existence of pressure.

DISCUSSION.

Dr. M. Allen Starr: Headache is such a common symptom that it seems a rather serious matter to recommend such a severe operation as trephining, and yet, as these cases of Dr. Folsom's certainly show, there are some cases in which we should come to this as a last resort. I have recently had such a case which presents some features of interest, and will mention it here, inasmuch as it is quite comparable to several of the cases related by Dr. Folsom.

A young man was struck upon the head four years ago, and since that time had suffered very intensely from constant pain at the seat of injury and his disposition had changed very much, as in the patients whose histories were related by Dr. Folsom, so that it was perfectly impossible for

his family to get along with him. From being a good-natured, fairly intelligent boy, he had become a perfect little devil. He was eighteen years of age at the time of the blow, in 1890, and during the years of his trouble, from eighteen to twenty-two, he had become a practically useless member of the community, and the family thought it was necessary to have something done. He had been under every possible form of a careful medical treatment when he was brought to the Presbyterian Hospital, New York, in February of this year. The boy, in addition to the pain and this change of character, was subject to attacks which I can only describe as comparable to the epileptic psychical equivalent, attacks of rage in which he would act in a maniacal manner, these attacks coming on about once in ten days, lasting an hour, during which time he was perfectly ungovernable, and after an attack had no recollection of what had occurred. He had no real fits, no petit mal. Examination of the boy revealed the existence of a cicatrix over the upper portion of the parietal bone on the left side, and a manifest scar on the surface of the bone, a slight depression. I examined him carefully with a view to any localizing symptoms or any actual brain symptoms, but failed to find any, and therefore Dr. McCosh in operating followed entirely the surgical indication of trephining at the position of the pain, which coincided with the position of the cicatrix.

Now I will say right here that my experience is that cicatrices in the scalp and in the skull do not as a rule give rise to a very great amount of pain. I have seen a great many cases of traumatic epilepsy and a great many cases of traumatism of the scalp in which other cerebral symptoms have developed, but pain at the seat of the injury is, in my experience, the exception and not the rule.

After the bone was exposed a slight depression was found in the external table. After trephining a disk of bone 1¼ inches in diameter, no fracture in the internal table, no adhesion of the dura to the bone, and no apparent congestion were found. The dura was divided and laid back, and then it was evident that upon the cortex of the brain there was a very great and abnormal increase in the amount of vascular tissue. The veins of the pia were enormously increased in number over a small area of about the size of a 25-cent piece and pulsated very forcibly. In other words, we had cut down upon a small angioma. The veins going to it were ligated, and it was taken away. There was very little affection of the cortex of the brain. It was thought best to puncture with a hypodermatic needle in three directions under the wound, as possibly there might be a cyst beneath the cortex, inasmuch as in a number of cases of traumatic epilepsy I have found such cysts; beneath the cortex nothing was found. The boy made a good recovery, has been entirely free from headaches, his disposition is tractable and natural, he is entirely free from the attacks of psychical epilepsy, and is in every way a new and better boy, and we believe that we have undoubtedly removed the headaches permanently.

I will mention here an observation that is of a great deal of interest in connection with the case. The trephining was done over the upper part of

the parietal region of the brain, involving the superior parietal lobule in its posterior part at least two and one-half inches beyond the fissure of Rolando, clearly away from the motor centres of the brain. For six weeks subsequent to the operation the boy had an absolute loss of muscular sense in the right hand and arm below the elbow, the most complete condition of inco-ordination I have ever seen, and also a total loss of the sensation of the position of his fingers and hand in space. It was perfectly impossible for him to reproduce in his left hand any position given to his right hand passively with his eyes closed. There was no disturbance, whatever, of motor power, no disturbance of touch, temperature or pain-senses. Those powers were all normal, but there was a total loss of muscular sense. It is the only case, I believe, that is on record in which a cortical lesion has produced a loss of muscular sense alone, and it settles a disputed question among neurologists and psychologists as to the existence of muscular sense as separate from motion and sensation.

CLINICAL REPORT OF TWO CASES OF RAYNAUD'S DISEASE.

By FREDERICK P. HENRY, M.D.,
OF PHILADELPHIA.

Case. I.[1] Patrick M., aged fifty-five years, native of Ireland, laborer, was admitted to the Philadelphia Hospital, November 11, 1893.

Family history. The patient's father died at sixty-five, of asthma, and mother at seventy-five, of "old age." Two brothers have died—one at thirty-five, of unknown cause, and the other at twenty-two, of smallpox. Three sisters died in childhood, of measles and smallpox. Two brothers still living and healthy. He knows of no hereditary disease in his family.

Previous history. He had smallpox and measles in infancy, malarial fever at eight years of age, doubtful left-sided pleurisy twelve years ago. Has used alcoholic liquors in moderate amount, average from two to three glasses of beer daily, but would occasionally drink to excess. On the other hand, months would sometimes pass without any indulgence in either beer or spirits. The patient has never had any kind of venereal disease. For the past six winters he has been subject to a severe cough, which has regularly caused the loss of a few pounds in weight. During the spring and summer the cough disappeared and the loss of weight was regained. The summer of 1893 was an exception to this rule. In January, 1893, he acquired a "cold," which has been with him ever since. The cough occurs in paroxysms most severe in the morning, and is attended with a yellowish, scanty, and tenacious expectoration. There has been neither hæmoptysis nor night-sweats. In August, 1893, the patient noticed that his urine was of a deep-red color during the afternoon. This bloody appearance of the urinary secretion was present almost continuously for about one month, but varied somewhat in intensity. One morning in October, 1893, after the patient had been much exposed to cold, he noticed that the helix of both ears was of a deep-blue color. This discoloration continued about two hours, during which the ears felt cold and were painful. Since the last mentioned date these attacks of local asphyxia have recurred on each exposure to cold. At first the signs of circulatory disturbance were more marked in the right ear, but later the left ear became the more involved, and about December 15th, a

[1] For the notes of this case I am indebted to Dr. Louis Préfontaine, resident physician.

small portion of the border of its helix became gradually converted into a dry, black sphacelus.

December 25, 1893. The tip of the nose became cyanotic early in the morning on exposure to cold, and has presented the same appearance nearly every morning since. On January 20, 1894, the second and third fingers of the right hand as far as the metacarpo-phalangeal joints became deeply cyanosed on exposure to cold in the morning. This "local asphyxia" has extended to the remaining fingers and to the first phalanx of the thumb of the same hand, but did not at first involve the left hand.

The blood was examined by the resident physician, Dr. Préfontaine, on February 9, 1894. Number of red corpuscles, 2,900,000; hæmoglobin, 43 per cent.; white corpuscles not increased in number. No tubercle bacilli could be detected in the sputum.

February 10, 1894. The patient was exposed for a few minutes to the morning air in order to make him more fully illustrative of a clinical lecture on Raynaud's disease which I delivered at the Philadelphia Hospital at 10 o'clock. The experiment was highly successful, the helices of both ears, the tip of the nose, the fingers, and the pulp of thumb of the right hand, and the first fingers of the left hand becoming deeply cyanotic and remaining in the same condition for nearly an hour. At 3.30 the same afternoon he passed four ounces of urine of a deep cherry-red or reddish-brown color, which reacted imperfectly to the guaiacum test for blood pigment.

11*th*. Cyanosis of ears and nose.

12*th*. Cyanosis of ears and nose. At 9.30 voided three ounces of reddish-brown urine, which did not respond to Gmelin's bile test, but gave the reaction to Mahomed's test, and contained a few red blood-corpuscles. In the afternoon the urine was of a normal appearance, but contained about 7 per cent. of albumin, roughly estimated. Its specific gravity was 1021.

13*th*. Urine still darker than that of yesterday morning, reacting similarly, and containing a very few red corpuscles. It also contained a few short, rather broad hyaline casts, stained with pigment. Albumin, 35 per cent. by volume. The afternoon urine was perfectly normal in appearance and gave similar reaction; it was free from casts and contained about 9 per cent. of albumin; specific gravity, 1023. The cyanosis this morning was comparatively slight.

14*th*, 9 A.M. Urine brownish-red, but not so dark as yesterday, acid, no bile reaction, no blood-cells or casts; contains a few large, flat epithelial cells; albumin abundant, apparently 30 per pent. by volume; quantity voided too small for specific gravity test; free from sugar. A specimen sent to Prof. Marshall, of the University of Pennsylvania at 12 o'clock was of a faint brownish-red hue; much lighter than in the morning; no blood-cells in specimen; did not respond to bile test; free from casts; specific gravity, 1030; reaction acid; albumin, 15 per cent. by volume; free from sugar. 2.30 P.M. Urine amber colored; no sediment; specific gravity, 1027; acid; a trace of albumin; no bile or sugar present; no casts found under the microscope.

15*th*. Cyanosis slight and limited to ears and nose. The urine passed at 7.30 A.M. was of normal appearance, free from sediment, of specific gravity 1020, and contained no albumin, casts, or blood corpuscles. It was acid and free from sugar. 11 A.M. Urine brownish-red, precisely like that passed at 12 o'clock the day before; sediment slight; specific gravity, 1026; acid; contains 15 per cent. by volume of albumin; free from casts, blood-cells, and sugar. A specimen sent to Dr. Marshall. 3.30 P.M. Urine of a cherry-red tint; acid; specific gravity, 1025; distinct ring with Heller's test; no cells or casts. 7.45 P.M. Urine normal in all respects, specific gravity, 1021.

16*th*, 9.30 A.M. Urine of same color as specimen voided yesterday at 11 A.M., and similar in all respects. 12.30 P.M. Urine darker than at 9.30; acid; specific gravity, 1027; free from blood-cells and casts; contains about 12 per cent. by volume of albumin. 3.40 P.M. Urine entirely normal in appearance; free from albumin, casts, and cells; specific gravity, 1022. This morning the cyanosis was slightly marked on the nose and ears and absent from the fingers. It persisted, however, longer than usual, being as well marked at 5 P.M. as at any time during the morning. The weather was quite cold. To-day Dr. Marshall sent the following report: "The spectroscope fails to show the presence of blood-coloring matter in Patrick M.'s urine."

17*th*, 7.30 A.M. Urine normal. 10 A.M. Urine of light-brownish tint; acid; specific gravity, 1022; no reaction with Mahomed's test; no casts; trace of albumin. Cyanosis is very slight to-day, affecting mostly the left ear, point of nose, and right ear, and absent from the hands. 4 P.M. Urine normal in all respects.

18*th*. Urine shows no change to-day; cyanosis slightly less than yesterday and in some areas.

19*th*. Urine normal in color and free from casts, cells, and albumin, although the cyanosis was more pronounced than yesterday in the ears and nose, and was perceptible in the fingers for a short period in the morning between 8.30 and 8.50. On the patient's rubbing his hands briskly it disappeared.

21*st*. The patient was allowed to go out on a pass for forty-eight hours. On his return he reported that on the morning of the 22d, which was very cold, his toes up to the metatarso-phalangeal joints were deeply cyanotic, as well as his nose and ears. His urine also was red during the two mornings of his absence from the hospital.

24*th*. A cold morning, but the patient keeps himself warm near the heater, so that the cyanosis is but moderate and limited to the nose and ears. The urine is normal in color, acid, of specific gravity 1023, and contains neither albumin, casts, nor blood-cells.

The urine was examined almost daily up to March 16th, when the patient left the hospital. It is unnecessary to give the details of these examinations, since they are precisely similar to those above recorded. The cyanosis was of daily recurrence, but varied greatly in severity and extent; on the other

hand, the albuminuria was markedly intermittent, being invariably present when the urine was of a deep brownish-red hue, and greatly diminished or absent when it approached or reached the normal color. The contradictory results of the examination of the urine for blood-coloring matter are inexplicable. The gross appearances of the secretion during the paroxysms of "local asphyxia" were precisely those of hæmaturia or hæmoglobinuria, and yet no absorption bands were perceived on spectroscopic examination. On the other hand, on several occasions the reaction of blood was obtained with the guaiacum test. As is well known, the late Dr. Mahomed, of London, claimed that this test would show the presence of hæmoglobin when the spectroscope failed to detect it. He stated, however, that it was not applicable to urine which responded to the ordinary tests for albumin. In the case of Patrick M. the spectroscope failed to detect blood-coloring matter, and yet in the same specimen, which was highly albuminous, the guaiacum reaction for blood was distinct. On February 23, I took a specimen of the urine to Prof. Henry Leffmann, who kindly examined it and sent me the following report:

"I made several experiments to-day with that sample, and got the guaiacum reaction for blood-coloring matter very plainly. I rendered the liquid acid by acetic acid, which, of course, caused much effervescence and produced a flocculent precipitate. This precipitate gave the blood reaction very strongly. I found that neither reagent alone nor when mixed, without adding some of the sample, gave any color."

Dr. Leffmann's examination of the urine with the spectroscope gave negative results. A specimen was also examined by Dr. Cattell, assistant pathologist to the Philadelphia Hospital, who reported that it reacted in thirty seconds to Almen's test for blood-coloring matter.

When I went on duty at the Philadelphia Hospital on February 1st I found Patrick M., in a ward assigned to phthisical patients. It has already been mentioned that tubercle bacilli were not found in his sputum. I examined his chest with the utmost care, and found neither dulness on percussion nor any auscultatory sign of consolidation or cavity. Sonorous râles were audible all over the chest, and were more marked during expiration, which was prolonged. The thoracic expansion amounted to only one inch and a half, the chest measuring at the height of a forced inspiration thirty-six inches, and at the end of a forced expiration thirty-four and one-half inches. There was a distinct history of attacks of paroxysmal dyspnœa for several years past, and taking this into consideration with the physical signs just mentioned, I concluded that the condition of the lung was one of moderate emphysema, dependent upon asthma and associated with chronic bronchitis. This history of previous asthmatic attacks which, I repeat, is confirmed by existing signs of emphysema, is extremely interesting, inasmuch as it demonstrates a tendency to spasm of unstriated muscle in other tissues besides the arterial. The heart, it should be stated, showed no signs of disease.

On March 16th the patient left the hospital and gave a false address, so

that my efforts to keep him under observation were thwarted. A few days before he left, the necrosed portion of tissue dropped from his ear, leaving a clean-cut semilunar loss of substance in the helix.

On April 13th, he came to my office and reported that he had been very poorly since leaving the hospital, especially during the recent cold and damp weather. The left ear was of a dark-purple color, but contained no gangrenous patches. The nose, right ear, and hands were of normal appearance. I examined his blood with the following result:

Number of red corpuscles per cubic millimetre, 3,166,666; hæmoglobin, 60 per cent.; white corpuscles not increased in number. The patient passed about two ounces of turbid, deep reddish-yellow urine, which was acid, of specific gravity 1030, and contained a trace of albumin (Heller's test). It was free from sugar. This sample was examined for blood-coloring matter by Dr. Leffmann, but with negative results.

Case II.[1]—Elizabeth R., aged seventy-seven years, born in Maryland, a widow, formerly occupied with indoor and outdoor farm work. Her mother died at fifty years of age of some acute disease characterized by flooding and vomiting. Two sisters died from the results of miscarriages; two brothers died of pleurisy, and two children of pulmonary phthisis. She had excellent health in early life. Since the age of twenty has had chronic rheumatism, recurring every winter in the right shoulder and arm. There are nodosities in certain of the phalangeal joints. She has had frequent attacks of gastro-intestinal disturbance which she terms cholera morbus. No history of malaria or syphilis can be elicited. She has never been addicted to the use of alcoholic liquors. At the time of the menopause she had a severe uterine hemorrhage, and has since, at long intervals, been troubled with metrorrhagia. The patient has been troubled with local symmetrical disturbances of circulation for the past twelve winters. For a longer time than this, however, the end of her nose had been rough during the winter months and discolored (purplish) when cold.

In the winter of 1881–82, while exposed to a cold wind, the helices of both ears became painful, and when she reached home it was noticed that they were swollen and black. This painful and discolored condition of the ears has recurred each winter. For the past two winters there have been symmetrical areas of cyanosis upon the cheeks, which, upon exposure to cold, become very blue and painful. In December, 1893, after an attack of influenza, the signs of local asphyxia reappeared in the old areas of invasion, and similar disturbances of circulation manifested themselves on the backs of the hands, the wrists, and the lower forearms. At the same time large elongated bullæ appeared on the inner side of each foot, running parallel with the first metatarsal bone and extending the greater portion of its length, and one on the outer malleolus of the left foot. It was on account of the last-mentioned lesion that this patient was admitted to one of the surgical wards under the care of Dr. John B. Deaver. One of the resident

[1] From notes taken by Dr. Lucas, resident physician.

physicians who had seen Patrick M. (Case I.), and who knew of my interest in the subject of Raynaud's disease, informed me that, in his opinion, there was a case of the affection in one of Dr. Deaver's wards. I found his diagnosis correct, and on applying to Dr. Deaver the case was transferred to me. I take great pleasure in expressing my thanks for the opportunity of studying this case to Dr. Deaver, and to his assistant, Dr. Kleinstuber.

Condition on admission to medical ward, March 2, 1894. The patient's general complexion is decidedly pale. The skin of the end of the nose, including an area about the size of a nickel, is thickened, indurated, and verrucous, and surrounded by a cyanotic border. On both cheeks are several large copper-colored spots arranged with almost absolute symmetry, and well represented in the sketch which I pass around for inspection. Precisely similar spots can be seen on the dorsum of the hands, the wrists, and the forearms. The helix of each ear is swollen, blue and tender, and contains a small black area of necrosed tissue. Upon the inner side of each foot there is an elongated red spot which indicates the former situation of the bullæ above mentioned. On the outer malleolus of the left ankle there is a cyanotic area, in the centre of which is a shallow, granulating ulcer about the size of a half-dollar. The discolored areas above mentioned are all increased in size and deepened in color in the early morning when the temperature of the ward is comparatively low. The urine has shown nothing abnormal, although repeatedly examined for albumin, sugar, casts, and blood. The patient, however, claims to have passed urine at times resembling milk, at other times as dark as coffee. Careful physical examination has revealed nothing abnormal with lungs, heart, liver, or other internal organ. An examination of the blood showed the number of red corpuscles to be normal, and their percentage of hæmoglobin to be 75. They presented no noticeable alterations of size or shape. The white cells were not increased in number.

May 17. During the last month fresh gangrenous spots have developed in the ears (there are now three in each) and there are complaints of pain when the temperature falls but a few degrees. Both ears are more cyanotic than formerly. In other respects the patient's condition is unchanged.

These cases are typical examples of the affection described by Maurice Raynaud in 1862,[1] and since classified under the head of Raynaud's disease. When clinically complete, the affection is characterized by great pallor and coldness of peripheral parts such as the fingers, toes, nose, and ears, on exposure to cold, followed by intense venous congestion of the same parts, and eventually, if the circulatory disturbances continue, by well-defined areas of dry gangrene. These are the essential clinical features of the disease, but,

[1] De l'Asphyxie locale et de la Gangrène symmétrique des Extremités. Paris, 1862.

in addition, hæmoglobinuria, as in Case I., and scleroderma, as in Case II., have been observed in a few cases. Raynaud's thesis contains a report of twenty-five cases, of which twenty were of the female sex. The disease is most prevalent in early life, the great majority of Raynaud's cases occurring between the ages of eighteen and thirty. The same observer noted five cases of the disease in children between three and nine years of age. He therefore suggested the term "juvenile gangrene" as an appropriate one for the affection, but it is objectionable because it might be supposed to imply that the disease is limited to the young. Both of the cases I report are of individuals decidedly advanced in life.

A perusal of Raynaud's thesis makes it evident that he regarded gangrene as an essential feature of the disease, at least in its full development. The first chapter of his treatise, which contains forty-four pages and occupies more than one-fourth of the whole work, is devoted to what he terms spontaneous gangrene.[1] Nevertheless, among the twenty-five cases which it contains there are several in which the process did not eventuate in gangrene, but stopped at the stage of "local syncope," or "local asphyxia." It is evident, therefore, that the minor grades of the disease, the *petit mal*, so to speak, of this arterial spasm, to which renewed attention has been recently called by S. Solis-Cohen,[2] were thoroughly recognized by Raynaud. This is shown, besides, more explicitly in the introductory remarks of his thesis, in which occurs the following:

"My ambition would be rather to demonstrate that certain facts of gangrene of the extremities which one meets at long intervals in practice, and of which the strange appearance is apt to disconcert the most skilful, are in reality much less singular than one would be tempted to believe, and can be connected by intermediate steps with other facts much more common, and which only escape attention by their everyday occurrence."[3]

The chief theories of the cause of Raynaud's disease are: (1) that it is due to an endarteritis obliterans; (2) that it is due to peripheral neuritis; (3) that it is the result of vascular spasm. The last is the theory of Raynaud himself.

[1] It is headed "Quelques Considérations sur la Gangrène spontanée."

[2] "Vasomotor Ataxia," Amer. Journ. Med. Sciences, Feb. 1894.

[3] Barlow's translation of Raynaud's Thesis. New Sydenham Soc. 1888, vol. cxxi.

The early age of many of the patients, the intermittent character of the symptons, and the great rarity of the disease as compared with endarteritis, suffice to exclude the latter as a causative factor in its production. There can, I think, be no doubt that cases of symmetrical gangrene occasionally reported as examples of Raynaud's disease have an anatomical basis in endarteritis obliterans, but they are in my opinion spurious. A case of the kind referred to is reported by George W. Jacoby,[1] of New York, and is highly interesting from several points of view. The patient, a male, aged forty-two years, first applied for treatment on account of numbness and coldness of the fingers (local syncope). This was followed by local asphyxia of the same parts, and subsequently by gangrene, the entire third phalanx of the left medius eventually sloughing away. Later, the signs of interstitial nephritis (albuminuria, urine of low specific gravity, casts, hyaline and granular, and hypertrophy of the left ventricle) appeared, and about four years after he was first attacked the patient died in an apopleptic seizure. In this interesting case it is probable, as Jacoby states, that the primary lesion was an arterio-capillary fibrosis, which gradually invaded the vascular system, attacking the vessels of the kidney later than those of the hands.

Jacoby gives the notes of another case in which the asphyxia was limited to the hands, and in which a cure was effected by a prolonged course of anti-syphilitic treatment. The cause of the condition was, presumably, a syphilitic arteritis.

There is little to support the theory that peripheral neuritis is the cause of Raynaud's disease. In the first place, the rarity of the latter and the frequency of the former militate strongly against it. Secondly, the cases in which neuritis has been found post-mortem may be examples of mere coincidence, or, more probably, the neuritis was secondary to the local circulatory disturbance. A degree of asphyxia sufficient in its severe forms to produce gangrene might, in its lighter grades, readily lead to degenerative and inflammatory changes in the nerves of the affected part.

The theory of arteriole spasm is certainly the one that is most in accordance with the clinical phenomena. The disease is most

[1] New York Medical Journal, Feb. 7, 1891.

prevalent in females and in the young—*i. e.*, in those whose vasomotor system is most impressible. It occurs in paroxysms which are caused by the surest exciter of vascular spasm—cold. Finally, in several cases during the paroxysm there has been dimness of vision, which was shown by the ophthalmoscope to depend upon a contraction of the central artery of the retina and its branches, and in one recently reported by H. M. Thomas[1] the attacks of local syncope were followed by a chill, loss of consciousness, and convulsions. Such facts are in the highest degree corroborative of Raynaud's view, that the disease known by his name is due to an "enormous exaggeration of the excito-motor energy of the gray parts of the spinal cord which control the vasomotor innervation."

The symptom hæmoglobinuria, occasionally observed, is best explained by the theory of vascular spasm. The origin of the hæmoglobinuria may be twofold: it may be due to excretion of hæmoglobin that has been separated from the red corpuscles in the peripheral asphyxiated parts—nose, ears, and fingers—or it may be due to an asphyxia of the renal or other internal vessels. I incline to the latter view as most applicable to Case I., and for the reason that the hæmoglobinuria was the first symptom in the case. It will be recalled that the deep-red color of the urine attracted the patient's attention in the *summer* of 1893, about two months before the peripheral asphyxia was observed.

I freely acknowledge, however, that the facts are in favor of the view that in the majority of cases in which hæmoglobinuria is observed this symptom is dependent upon an excretion of hæmoglobin which has been separated from the red corpuscles in the peripheral asphyxiated parts. Hæmoglobinuria coinciding with hæmoglobinæmia of the blood of the asphyxiated fingers has been frequently observed.[2] On the other hand, hæmoglobinæmia may exist, and probably often does, without hæmoglobinuria. An instance of the latter kind is reported by Taylor and Colman.[3] The patient was a girl, ten years of age, who was subject to attacks of dead finger (local syncope) affecting the distant phalangeal joints. "Local asphyxia" was never observed. In blood with-

[1] Johns Hopkins Hospital Reports, vol. ii.

[2] For example, by A. T. Myers: Trans. Clin. Soc. London, 1885. Boas: Deutsch. Archiv für klin. Med., 1883. Bristowe and Copeman: Trans. Med. Soc. London, 1889.

[3] Trans. Clin. Soc. London, 1890.

drawn from the finger during an attack the liquor sanguinis was distinctly colored, while the red corpuscles were shrivelled and irregular in shape and many of them devoid of hæmoglobin. Neither hæmoglobinuria nor albuminuria was ever present. I regret that a more thorough examination of the blood taken from the fingers during the stage of asphyxia was not made in the first of my cases. It was examined but upon one occasion, and nothing abnormal was detected. It is probable that hæmoglobinæmia is frequently present without hæmoglobinuria. The spleen and liver are capable of storing up large quantities of hæmoglobin; in fact, according to Ponfick, it is not until the separated hæmoglobin amounts to one-sixtieth of the total amount in the blood that hæmoglobinuria occurs. Until the hæmoglobinæmia has reached this degeee, the attack, so far as the urine is concerned, is only manifested by albuminuria. It seems to me probable that paroxysmal albuminuria in other affections than Raynaud's disease may be but a symptom of a comparatively mild grade of hæmoglobinæmia.

The relation between Raynaud's disease and chilblains has been recently studied by Legroux,[1] and is worthy of further investigation. As this writer tersely remarks, chilblains do not come at will,[2] a predisposition is essential to their production, and he raises the question whether chilblains, local asphyxia, and symmetrical gangrene may not represent different degrees of a necropathic dystrophy, of which the most striking example is furnished by syringomyelia.

To those who have seen at least a single instance of Weir Mitchell's disease (erythromelalgia) it seems scarcely credible that it should have been confounded with the affection of Raynaud, nevertheless this has been done. I will content myself with stating here that the differences between them are radical.[3]

I have said nothing about the treatment of these cases because no systematic treatment was pursued in either of them. With the exception mentioned in the report of Case I, they were protected

[1] Annales de Dermatologie et de Syphiligraphie, 1892, tome iii.

[2] "N'a pas des engelures qui voudra."

[3] For the differential diagnosis between these diseases the reader is referred to Dr. Weir Mitchell's article on "Erythromelalgia." in the *Medical News* for August 19, 1893.

from cold and nourished as well as circumstances permitted. It was expected that with the approach of milder weather their condition would improve, and this expectation was fulfilled. It was my intention to test in one of the cases the effect of the electrical bath as recommended by Barlow and R. Glasgow Patteson,[1] and in the other that of the continuous administration of glonoin in small oft-repeated doses.

My report is nothing more than it pretends to be—a clinical one. I have made no attempt to analyze the numerous recorded cases, still less to separate the spurious among them from the genuine. Raynaud's disease is a paroxysmal affection, and, therefore, cases in which peripheral gangrene has followed injury of the part affected or has gradually supervened upon an obliterating endarteritis, as well as those in which the stages of local syncope and local asphyxia have been absent, are, to say the least, to be regarded with suspicion.

DISCUSSION.

Dr. Lyman: The lateness of the hour renders it impossible to discuss this most interesting paper. I merely wish to call attention to a point of relationship which I think is brought out by these cases, especially by the first patient, if we may trust the portrait which has been exhibited. It is evident from inspection of the portrait, as well as from the history given, that the patient was a victim of chronic arthritism. The second patient, if we may trust the portrait, exhibits similar characteristics. Both of these patients, I should say, from the physiognomy of the pictures presented, were arthritic subjects, and the relation between arthritism and the disease should be kept in mind. I have seen quite a number of cases of Raynaud's disease in which that relationship is very evident. The fact that a proclivity to irregular muscular spasm is one of the consequences of arthritism goes far to support Dr. Henry's hypothesis regarding the etiology of this disease.

Dr. Wm. Osler: Dr. Henry has referred to a case reported by Dr. H. M. Thomas from my clinic. It was very interesting, indeed, in this respect that the attacks occurred only during winter, always associated with epilepsy, and usually associated with hæmoglobinuria. In connection with the cerebral manifestations of the disease, we have also had under observa-

[1] Dublin Journal Med. Sci., vol. xciii.

tion a remarkable case in which with the local asphyxia, sometimes without, the patient has aphasia, sometimes with and sometimes without hemiplegia.

Dr. M. Allen Starr: The disease can be entirely outgrown. I had a little girl under my observation for three years, from 1884 to 1887. She came at the age of three. I have seen her recently, and she has entirely recovered from the typical condition of Raynaud's disease. In that case the most careful treatment by galvanic bath failed utterly.

Dr. W. H. Welch: As I understood Dr. Henry, he considers that hæmoglobinuria associated with cases of Raynaud's disease is referable to the vascular spasm. It is not at all clear to me how there can be a connection between hæmoglobinuria and arterial spasms. Is it not possible that the hæmoglobinuria in these cases belongs to the general type of paroxysmal hæmoglobinuria that follows exposure to cold. The experiments of Ehrlich and of Rosenbach indicate that the red blood-corpuscles in this condition are unstable and readily, under the influence of cold, give up their hæmoglobin. Is it not more probable that the corpuscles give up their hæmoglobin, in these cases described by Dr. Henry, from this cause, and that vascular spasm has nothing to do with it?

Dr. Henry: I think there is undoubtedly a greater vulnerability on the part of these individuals to such causes as dissolve the red blood-corpuscles than on the part of other people, but it seems to me also that the arterial spasm, the effect of which is to produce a marked venous congestion, sending back the blood into the venous radicles, thereby producing local asphyxia (the term signifying this condition of venous congestion which exists with this local alteration of the circulatory condition) is also concerned in the production of the hæmoglobinæmia. The hæmoglobinuria is a result of the hæmoglobinæmia. The blood coloring matter separated in the peripheral asphyxiated parts is excreted as foreign matter by the kidneys.

INVESTIGATIONS UPON COW-POX.

By STEPHEN C. MARTIN, M.D.;

Presented by Harold C. Ernst, M.D.,
of Jamaica Plain, Mass.

As some of the Fellows of the Association may recall, I presented to them at the meeting of 1890 a few brief notes of work done by Dr. Stephen C. Martin upon the infectious element of cow-pox. At that time the experiments were not sufficiently advanced to permit a detailed statement of the results to be made, and I, in common with everyone else interested, looked for a continuation and completion of them by him who originally undertook them. The purpose of the communication at that time was merely to note progress and to secure priority for Dr. Martin.

Unfortunately our hopes of the completion of the work as it was begun have been disappointed, for soon after that communication Dr. Martin was disabled by the illness that finally caused his death in the fall of 1893.' As will be seen, he left the following notes to me, and it has seemed eminently proper that they should be recorded in the *Transactions* of this Association, where the first note of his work made its appearance.

I give them with hardly the alteration of a word, but with the addition of the extract from the letter to the *Grocers' Guild*:

In the fall of 1888, with the desire of investigating the contagium vivum of cow-pox, and having no knowledge of the technique of bacteriology, I entered the laboratory of the Harvard Medical School for a course of instruction in the latter under Dr. Harold C. Ernst, its director. When I acquired sufficient familiarity with the methods of bacteriological work I began my experiments upon

the cow-pox, Dr. Ernst kindly giving me the facilities of the laboratory and in every possible way aiding and encourgaging me in my work.

My father, the late Dr. Henry A. Martin, had in the fall of 1870 introduced the practice of animal vaccination into this country and founded an establishment for the propagation of cow-pox virus. This latter he had superintended himself until the spring of 1873, when he gave it into my hands; and since that date I have maintained the disease (cow-pox) continuously upon an unbroken succession of calves. I had, therefore, unusual facilities for carrying on my experiments, together with a familiarity with vaccinia in all its phases in man and in the calf, gained by a more than twenty years' daily, almost hourly, experience, for to this subject I had devoted my whole professional life.

To quote from an earlier preliminary report of mine (see *Boston Medical and Surgical Journal*, December, 1893), I found that a large number and variety of bacteria obtained from vaccinal virus can be grown upon the various culture media. Experimenting with gelatin, glycerin-gelatine, milk-rice, agar-agar, and glycerin-agar-agar I obtained pure cultures of many varieties, none of which, however, produced cow-pox when inoculated upon the animal. I abandoned the use of all culture media except the hardened sterilized serum of bullock's blood (note: horse's blood equally good). With this, at a constant temperature of $37\frac{1}{2}°$ C., I have since conducted all my experiments. So soon as I adopted this course I got cultures that produced cow-pox, even after passing through several generations of culture-tubes. The blood-serum tube inoculated with virus from a vesicle on a calf and placed in the thermostat at $37\frac{1}{2}°$ C., would, at the end of twenty-four hours, exhibit an extensive white, creamy growth, with commencing liquefaction of the medium. The process would go on very rapidly till, on the seventh day, the contents of the tube consisted of a turbid liquid with a deposit of broken-down medium and bacteria at the bottom. On inoculating calves from these tubes on the seventh day I succeeded in producing vesicles of cow-pox, small and feeble, to be sure, but still showing the characteristics of true vaccinia.

I vaccinated no children directly from these cultures, but on

March 27, 1890, vaccinated two children with points taken from a vesicle produced from these cultures on a calf, and got in both typically fine arms (an account of these is given in Dr. Ernst's report at Washington. See *Transactions* of this Association, 1890, vol. v., p. 181). These tubes were, of course, not pure cultures, cover-glasses from them exhibiting a great variety of forms and sizes of bacterial growth, yet it was evident that among these various forms was present the specific germ of cow-pox; and the all-important fact was at last proved that this germ could be grown upon blood-serum at a constant temperature of 37½° C., and that after several generations of such cultures it still retained its pristine vigor. All that remained to be done now was to isolate from among these different germs that one that was the specific germ of vaccinia, and grow it in pure cultures. This presented difficulties, from the fact, proved by my previous experiments with glycerin-agar-agar, etc., that the germ would grow only on blood-serum, and therefore could not be isolated by plate-cultures.

On November 20, 1890, I inoculated three blood-serum tubes (A) in the following manner: Into a test-tube containing 10 c.c. of sterilized water I poured the contents of two capillary tubes of lymph taken five days before from a finely-developed seven-day vesicle of cow-pox (Beaugency) upon calf 1402. With a sterilized needle dipped into this mixture I drew nine lines upon the surface of the blood-serum (three lines on each blood-serum tube) without recharging the needle, my object being to secure as great separation as possible of the germs. These tubes were then put into the thermostat and kept at a temperature of 37½° C. On the third day in one of the tubes three widely separated colonies showed themselves on the surface of the blood-serum in the upper part of the tube, and a dozen or more smaller ones at the lower part; at the same time quite a deposit had begun to form in the condensation water. These colonies all presented the same appearance. They were white, and never increased much in size. Each colony occupied a little depression, which it had formed for itself by liquefying the medium about it. Later the liquefied blood-serum flowed down from the colonies, carrying the growth with it, and so producing liquefaction in its course and forming white lines occupying shallow eroded sulci running down into the condensation water.

At the bottom of the latter a heavy cloud settled, consisting for the most part of disintegrated blood-serum, while the upper portion of the water presented a remarkably clarified appearance. At the end of six days (November 26, 1890), I inoculated a second blood-serum tube (A1) from one of the isolated colonies on the upper part of the tube A, and placed it under the same conditions as the first tubes; and after that I kept up a continuous succession of cultures, all of which presented the same characteristic appearance. On December 13, 1890, I inoculated Calf 1 with points from tube A1 (see notes on experiments on calves and children), and on December 22d three children with lymph from vesicles produced by that inoculation; on December 31st one child with lymph from Calf 2. (Notes of results, etc., of these inoculations of calves and children given at length in "Experiments on Calves and Children," a copy of which is given below):

INOCULATION EXPERIMENTS.

CALF 1. (Pure cultures only.) November 26, 1890. Inoculated blood-serum tubes A1 from colony on blood-serum tube A. Kept in thermostat at 37½° C. for seven days, then in room temperature. *Microscopic examination.* Pure culture.

On December 12, 1890, charged six points with fluid and sediment of tube A1, and on December 13, 1890, inoculated Calf 1 in six places with same.

Temperature, 99.6° F.; fifth day, 103.4° F.; sixth day, 103.6° F.; seventh day, 103.8° F.; eighth day, 105° F.; ninth day, 101.4° F.

On the fifth day showed signs of taking in three places. On seventh day small vesicles in five places. Took points and cover-glasses from two of them, and (December 20th) inoculated Calf 2 in fifteen places on belly. On eighth day the vesicles (5 places) much more fully developed. Took points and cover-glasses. Ninth day the five places have become fine typical vesicles, perfect in every way. Took points, cover-glasses, and tubes. Microscopic examination of all the cover-glasses showed the bacterium in great abundance, apparently pure.

CALF 2. (Pure cultures only.) Red and white steer. December 20, 1890, 11 A.M. Upper side, 4 places, A2, blood-serum, sediment. Lower side, A2, blood-serum, sediment. Belly, fifteen places, A1, Calf 1, seventh day. On the eighth day (December 28th) only one vesicle (fine) on upper side. Three fine vesicles and one small one on lower side. The fifteen places on belly magnificent vesicles. Points and cover-glasses from all.

Temperature on second day 102.6° F.; on third day, 103° F.; on fourth day, 103.8° F.; on fifth day, 103.9° F.; on sixth day, 104.6° F.; on seventh day, 103.4° F.; on eighth day, 104.6° F.

Calf 3. Red and white heifer. Six months old. Pure culture. January 4, 1891.

Belly 2 places. A.
3 places. A1.
2 places. A3, b. s.
3 places. A3B.
3 places. C1 middle.

All showed effects, the least in the two places A3, b. s. One place A, one place A3B, and one place C1 middle, very fine typical vesicles, the others decided vaccinal effects. On January 13th took points from all except A3, b. s.

Calf 4. (1511). Black bull. Belly.

1 place, A4, top. Seventh day, vesicle.
Eighth day, fine.
4 places, A4, sediment. Seventh day, 2 good, 2 dubious.
1 place, C. Seventh day, good; eighth day, fine.
1 place, 2A, top. Seventh day, good; eighth day, very good.
1 place, 2A, bottom. Seventh day, good; eighth day, very good.
2 places, C2. Seventh day, good; eighth day, very good.
3 places, A3. Three very fine vesicles.
3 places, A1 3. 2 fair; eighth day, 2 good.
3 places, A3B3. 3 very fine vesicles.
3 places, C1 3. 3 very fine vesicles.

C.

On December 5, 1890, inoculated calf 1505 in four places with points charged from blood-serum tube, C (c. a.)

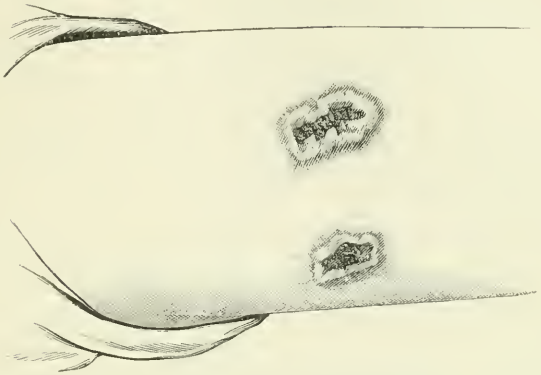
On eighth day, December 13, 1890, one fine vesicle and one very slight effect. From these two inoculated (December 13th) Calf 1506 in six places; on seventh day six perfect vesicles. Microscopic examination of cover-glasses showed the bacterium in abundance but contaminated (?).

December 22, 1890, 12.30 P.M.—Vaccinated with points taken from Calf 1 on seventh, eighth, and ninth days.

Christopher Johnson, 7½ years old, ninth day.
Walter Johnson, 5½ years old, eighth day.
Margaret Johnson, 3 years old, seventh day.
December 26.—All taking.
December 29, 11 A.M.—All six beautiful vesicles; no sign of areola.
December 30, 10.30 A.M.—Magnificent vesicles; no sign of areola.
12.30 P.M.—Areola just beginning on C. J.; no sign on others. Cover-glasses from W. J.
December 29.—C. J.'s arm photographed.
December 31.—C. J.'s arm photographed.
11 A.M.—*Well developed areolæ in all the arms.*

January 8.—Vaccinated these three children with active cow-pox virus.
January 15.—No sign whatever.

Fig. 1.



Arm of Christopher J., December 31, 1890.

December 31, 1890.—Vaccinated Ernest Long, aged two years and one month, in two places with points from Calf 2 (A2, b. s.)
January 8, 1891.—One fine vesicle; no effect in the other place.
Same date, vaccinated in one place with active cow-pox.
January 15.—Not the slighest effect from the last.

Up to this time I had been strangely misled by a method of staining that I had used. In many attempts to find germs in cow-pox vesicles I had little or no success, although I tried every method of staining that I could think of, until aniline water solution of fuchsin raised to a very high temperature showed large quantities of very minute bodies about the size of granules composing "mast cells." These I mistook for very small cocci. Not only did I get this appearance in sections, but also in cow-pox virus. Not only I, but several very careful and experienced bacteriologists as well, were deceived by it, and I felt certain that at last I had found the long-sought-for germ of cow-pox. Strangely enough, the few cover-glasses that I made from my cultures A, A1, etc., which I stained by this method, had no real germs upon them, but showed this supposed minute coccus in great abundance. I was now happy in the thought that I had at last attained the object of my search, for I found an organism which was invariably present, not only in cow-pox lymph and sections of the vesicles,

but also in great abundance alone, by itself, in my cultures, which should by all laws of bacteriology be, and had every appearance to the eye of being, pure, as well as in the lymph from the vesicles produced on the calf and arms by these cultures.

One or two points about this coccus, however, arose to shake my confidence in it, and upon careful investigation I found that it was not a coccus at all, but simply a deposit caused by the method of staining, and that the same appearance could be produced upon a perfectly clean cover-glass by using the same stain. I now made fresh cover-glasses from my cultures, used a simple solution of fuchsin for a stain, and found present a small coccus and a small bacillus. One of these two forms must be the specific germ. Here, my friend, the late Dr. John A. Jeffries, than whom no better bacteriologist existed in this country, rendered me most important and signal assistance. He kindly offered to help me separate, and make pure cultures of, these germs. I gave him my second tube in the series A1 to start with. He made a series of most thorough and exhaustive experiments, according to the strictest bacteriological laws, and demonstrated conclusively that according to all the canons of this science these two forms were but different stages in the development of one and the same bacterium. See p. 3, paragraphs 4, 5, and 6 of my report to *Grocers' Guild*, London. This reads as follows:

"The bacterium varies in form according to the various conditions of its nutritive environment and the consequent rate of its development. The most constant and prevalent form is a short, fine bacillus with rounded or nearly square ends. Those parts of the culture where the nutriment is apparently exhausted show the same bacillus in short chains, longer bacilli, and bacilli much enlarged at one end or in the middle, as if in preparation for spore formation. Where the nutrient medium is fresh the plant divides more rapidly and forms very short bacilli, and often even a pure micrococcus form. The latter, too, is frequently seen forming chains of five or six. Chains are observed made up partly of bacilli and partly of micrococci. The micrococcus form is found for the most part in early colonies at the upper part of the culture-tube, where the nutrient medium retains its freshness by the constant draining away of the liquefied and exhausted portion. On the other hand, where this abounds, as in the sulci, and pockets and condensation water into which these drain, the bacilli greatly predominate, and the "balloon" forms appear. Cover-glasses of the growth stain well after a few seconds' exposure to Ziehl's carbolic acid

fuchsin solution. I have repeatedly inoculated tubes from isolated colonies that manifestly grew from a single bacterium; and the resulting cultures have invariably shown all the forms enumerated above."

FIG. 2.

Oc. 8, obj. $\frac{1}{12}$ oil im. May 5, 1894.

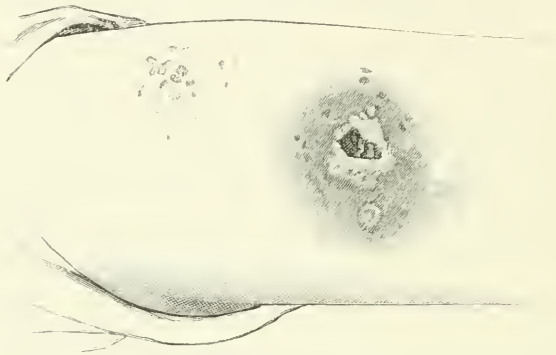
My own experiments, carried on *pari passu* with his, went to confirm his results, and it was now conclusively proved that the cultures I had been working with were pure, as I had supposed before the dual form confused me, and it is just here that Dr. Jeffries's superior knowledge of bacteriology came to the rescue.

In the meantime I had continued my series of cultures, and on the 21st of March, 1891, I gave my friend, Dr. Edward T. Williams, of Roxbury, Mass., two points charged with sediment of culture tube A10a4, which under the microscope showed only the two forms which I had come to recognize as the true germ of cow-pox. The genealogy of this tube is as follows: A10a4 inoculated from A10a3, from A10a2, from A10a1, from A9a, from A8a, from A7a, from A6a, from A5a, from A4, from A3B, from A2, from A1, from A. It was therefore the fourteenth generation of blood-serum culture from original stock of cow-pox virus. With this Dr.

Williams vaccinated Georgiana MacFarland (aged four years) on March 21, 1891, with the result March 28, 1891, of a typical vesicle of cow-pox perfect in every way.

This was the last and conclusive experiment needed in the investigation. Perfect vaccinia in man had been obtained by inoculation of a germ in the fourteenth generation of pure culture in the laboratory.

FIG. 3.



Arm of Georgiana MacFarland. Vesicle from pure culture.

I would here state that Dr. Williams had not made a vaccination or had any vaccine virus in his possession for over a year; that the lancet which he used had not only been freshly ground but thoroughly sterilized in an alcohol flame before making the vaccination. One or two important points should be noted. As my experiments on calves will show (see note), I obtained upon the animal typical vaccinal effects from all of the culture tubes that I used—varying from very fine to quite feeble and poorly-developed vesicles. But no matter how feeble the vesicle may have been, the lymph taken from it would, on the next calf, produce fine typical vesicles. In all the numerous instances in which I vaccinated a child with lymph taken from a vesicle produced on the animal by inoculation with cultures, I obtained typical vaccinia. I have vaccinated ten children with the pure culture, but in no case have I succeeded in getting the desired effect, Dr. Williams' case of the child MacFarland giving the only successful result as yet obtained in man.

Calves 1 and 2 were vaccinated from culture tubes solely. The other calves used in the series of experiments were at the same time vaccinated with the regular cow-pox. But the culture inoculations

were widely separated from the others, and my experience with the vaccination of animals leads me to say with confidence that it is impossible that the presence of the cow-pox virus should in any way have modified the effect of the culture. To meet another objection that might possibly be raised, viz., that these animals were vaccinated and left in quarters impregnated with cow-pox, where the propagation of the same had been carried on for twenty years, I would say that in all my former experiments with cultures grown upon gelatin, agar-agar, etc., I had obtained no results whatever—that cow-pox virus from different sources inoculated simultaneously upon the same calf produces results varying all the way from fine vesicles to absolute failure—and that as a control experiment I had in several instances made upon the calf inoculations with simple water among those made with regular cow-pox virus which I propagate, and the result has invariably been negative. All of which proves my assertion that the germ inoculation could have been in no wise modified by the presence of cow-pox in the animal's system.

Briefly stated, the results of my investigations are as follows:

1. The germ of cow-pox is a bacterium.

2. This bacterium is, in different stages of development, in the form of a coccus or of a bacillus.

3. It can be isolated and grown in pure culture on blood-serum at the temperature of the blood.

4. Inoculation on the calf from such cultures readily produces the typical cow-pox, while inoculations in man have, so far, produced typical cow-pox but once in eleven times.

All that remains to be done now is to find under what conditions to grow the pure culture, that it may be uniformly relied upon for vaccination in man. I had hoped to complete this work myself, but as that is now out of the question I present this paper, written under stress of great pain and limited time, to show how far my work has gone. And I shall ask Dr. Harold C. Ernst, Director of the Laboratory of the Harvard Medical School, where all my investigations have been carried on, and who has been kept informed of the results of my work from the beginning, to add his signature as an indorsement of the same. To him I give all my slides, cultures, etc., with a copy of my notes, in the hope that he will see fit to carry on the work. (Signed) STEPHEN C. MARTIN.

JANUARY 29, 1893.

It is difficult to see, gentlemen, what more there is for me to say in connection with these notes, written as Dr. Martin says, a few days before undergoing a severe operation, and concluded only the night before. So far as my knowledge extends, they contain an exact summary of the work that he did in my laboratory, and which I followed as it progressed. I saw the vesicles on the calves and on the children, as well as the cultures; and specimens from these latter I lay before you for your inspection.

The full text of his letter addressed to the Grocers' Company in London may be found in the *Boston Medical and Surgical Journal* for December, 1893.

DISCUSSION.

Dr. W. H. Welch: The results reported in this paper are very important, if true. Of course, others have made observations in much the same way, with negative results. The methods are simple and easy to repeat, and we shall, of course, learn whether these observations are confirmed by others. The question is left by Dr. Martin in that condition where the work needs to be repeated by somebody else; it needs confirmation.

Dr. A. C. Abbott: I have nothing especial to add; I have had no practical experience in the matter. It is a very interesting piece of work, and there are one or two points in connection with it that make me feel that subsequent observations might modify the results.

Dr. G. M. Sternberg: I would like very much to have these experiments repeated by an accomplished bacteriologist. There ought to be no difficulty in confirming the experiments, if they are reliable.

Dr. H. C. Ernst: The work, as you know, was carried on in my laboratory for months, and I certainly saw the colonies that apparently did produce these results. One reason for presenting the work here is to secure confirmation or refutation. I was unable to see any fallacy. I used to talk with Dr. Martin very carefully about his work, and would question him every way I could, but I could not detect a fallacy. I have seen the vesicles produced constantly upon calves. I dare say many of the physicians present have used Dr. Martin's vaccine virus that has been produced by these pure cultures. Much of his active virus that was sent out for the last two years from his establishment, was produced on the calves by these cultures. I have his slides—all that are left of them—and these forms are on those slides. I have seen this definite liquefaction of the blood-serum going on as he describes.

MODIFICATION, TEMPORARY AND PERMANENT, OF THE PHYSIOLOGICAL CHARACTERS OF BACTERIA IN MIXED CULTURES.

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THE interest which is manifested by medical science in the occurrence of varieties of well-defined species of bacteria is somewhat different from that aroused by the philosophical contemplation of the mutability of species. The variability of pathogenic bacteria is a most suggestive subject when brought together with the phenomena presented by the transmission of infectious diseases and the rise and decline of epidemics. We possess, however, very little positive information on this subject as yet. Before generalizing we must first demonstrate the evolution of races and determine to what agencies they owe their existence. The following experimental facts are presented with the hope that they may contribute something toward the solution of this problem.

To trace the development of ideas concerning the variability and transmutability of bacteria would be equivalent to writing a fairly complete history of microbiology. I therefore content myself with the bare mention of the more recent methods used to produce varieties before entering upon the more restricted theme of this paper. These methods consist in the passage of bacteria through a series of animals (Coze and Feltz, Davaine, Pasteur and his pupils), exposure to heat (Pasteur), to compressed air and oxygen (Chauveau), to chemicals of various kinds (Chamberland and Roux, Troje), to sunlight (Laurent), and the fluids of the living animal (Gramatschikoff). In 1891 I quite accidentally discovered that certain pathogenic bacteria which had resisted tenaciously the modifying influ-

ence of several of the methods just cited were markedly changed in impure or mixed cultures. Before this date some observers had been studying the mutual effect of bacteria on each other when multiplying intermingled in the same culture medium. These studies were pursued mainly to determine the capacity of one or the other species to survive in the struggle for existence.

Charrin[1] inoculated actively growing bouillon cultures of the anthrax bacillus with the bacillus of blue pus in order to observe any change in the virulence of the former. For the first six days this remained unchanged. Subsequently, inoculated animals remained alive longer. When two weeks old, the mixture was fatal after nine or ten days. Involution forms also made their appearance. The attenuation was limited to the bacilli actually influenced,and was not transmitted, for the original virulence promptly returned in pure cultures.

Blagovestchensky[2] studied the mutual influence of the same species by a somewhat different process. Agar plates were inoculated in the form of intersecting lines with anthrax and blue pus bacilli, so that at the points of intersection both species would grow intermingled. After seventy-two hours at 33° to 34° C., the bacilli of blue pus had multiplied vigorously, and the anthrax bacilli had begun to degenerate. This degeneration was followed by a total disappearance of the anthrax bacilli.

Vincent[3] studied the effect of impure cultures on the typhoid bacillus. In bouillon at the ordinary temperature inoculated simultaneously with—

B. prodigiosus and B. typhosus, the latter disappeared in . . . 3 days.
B. coli communis and B. typhosus, the latter disappeared in 8 to 11 "
P. vulgaris and B. typhosus, the latter disappeared in . . . . 17 "
P. vulgaris and B. typhosus at 37.5° C., the latter disappeared in . 60 hours.

In a more recent communication d'Arsonval and Charrin[4] introduce the subject anew by demonstrating the inhibitory action of *B. pyocyaneus* on yeast. At 37° C. only very little CO_2 is formed in mixed cultures. At 10° C. the inhibitory action is very slight.

Mühsam and Schimmelbusch[5] have very recently studied the action of various bacteria on the pigment-producing function of *B. pyocyaneus* when multiplying in the same culture tube. In most cases the normal pigment was replaced by other colors.

These investigations illustrate the antagonism between bacteria multiplying together. A mutually favoring action has only been noted by Vincent,[6] who states that typhoid bacilli and streptococci get along very well together. This does not imply that they actually favor each other, however. In this connection it might be well to quote the curious, unconfirmed statement of E. Salkowski,[7] that gelatin plates made with one c.c. of drain and other polluted water present larger colonies than plates made with only 0.05 c.c. This observation he interprets by assuming a mutually favoring action of the different species.

Closely related to the problem of the antagonism of living bacteria is the one which seeks to determine the effect of growing one species in a medium impregnated with the metabolic and other products of some other species. Garré[8] was the first to call attention to the subject of antagonism. He allowed one species to multiply on gelatin, and subsequently cut out the growth in order to make room for another species. The antagonism was quite marked in the case of some species, and he was inclined to see in this new fact the germ of important applications to the explanation of disease processes.

Sirotinin[9] took up the same subject on a more extended scale. He sterilized full-grown gelatin cultures of given species either by boiling or by filtration. To the boiled culture fresh gelatin was added, and then inoculated with the second species. The filtered gelatin was mixed with agar to prepare it for the second inoculation. The secondary cultures obtained were in most cases even more vigorous than in control tubes. This he explained by the increased alkalinity of many of the sterilized cultures. He concludes that the antagonistic or favorable effects produced by bacterial products are largely due to the development of a more acid or a more alkaline reaction rather than to any specific substance formed by the primary culture. He also states that several successive transfers of *B. anthracis*, *M. tetragonus* and *B. sputigenus* on such modified gelatin did not alter their virulence.

De Freudenreich[10] made a similar series of experiments. He inoculated a series of bouillon tubes with various species, and after a certain time passed them through the Chamberland filter. The series of filtrates were then reinoculated with a different set of bac-

teria. His results indicate that the products of certain pathogenic species (typhoid, anthrax, and fowl cholera) have little if any modifying influence on the second growth, while certain other species (*B. pyocyaneus, Spirill. chol. Asiat., B. phosphorescens*) have a marked effect in retarding or completely checking the multiplication of other species. In a more recent publication[11] the same author (probably influenced by the work of Sirotinin) is inclined to the view that while the reaction of the culture fluid has some influence it does not by itself account for the phenomena of antagonism.

Blagovestchensky[2] found that anthrax spores failed to germinate in sterilized bouillon cultures of *B. pyocyaneus*. In filtered cultures the spores germinated, but the resulting growth was feeble.

Charrin[1] also states that in filtered or sterilized cultures of *B. pyocyaneus*, anthrax bacilli underwent degenerative changes.

Sanfelice[12] obtained some startling results by cultivating a non-virulent or pseudo-tetanus bacillus and a pseudo-œdema bacillus in culture media impregnated with the products of the true tetanus bacillus. The pseudo-tetanus bacilli were reinoculated into fresh culture media five times after leaving the poisoned media before they lost the power to produce tetanus. The same was true of the pseudo-œdema bacilli. The author is inclined to explain this curious fact as an acquisition, by the non-virulent forms, of toxine-producing properties.*

Lorenz[13] inoculated the bacilli of swine erysipelas or *rouget* into filtered as well as sterilized cultures of other bacteria in order to produce attenuated varieties. His results were negative, with one exception. He obtained a growth in filtered and heated cultures of swine-plague bacteria which was modified both as regards the appearance of the culture and its effect on mice.

Nencki,[14] taking up the subject of mixed cultures from a some-

* After the completion of this manuscript my attention was called to a series of experiments similar to those of Sanfelice by Roncall (Dell' azione del veleno del bacillus tetani associato coi prodotti di coltura di alcuni micro-organismi patogeni e non patogeni. Annali dell' Institut. d'Igiene della R. Univ. di Roma, 1893). This observer found that non-pathogenic as well as pathogenic bacteria after growing for fifteen or twenty days on agar impregnated with the products of the tetanus bacillus produced in animals symptoms of tetanus followed by speedy death. When removed from the agar containing the tetanotoxines and passed through nine or ten tubes of sterile agar, the non-pathogenic species killed guinea-pigs after inoculation with toxæmia, the attenuated pathogenic forms produced a true septicæmia, and a virulent anthrax culture produced a more rapidly fatal disease, differing from the usual anthrax disease in certain features.

what different point of view, was the first to point out that by the associated growth of two species the products of fermentation may be different from those in the pure culture of either species. The mutual effect may be advantageous to either species or disadvantageous—a condition designated by him as enantibiosis in contradistinction to symbiosis. He generalizes further on the possible symbiotic relations of bacteria producing the so-called miasmatic-contagious diseases (Asiatic cholera, typhoid, diphtheria) with other bacteria to account for the still mysterious character of their activity.

v. Schreider,[15] continuing Nencki's observations, found the tox-albumoses from mixed cultures of diphtheria bacilli and streptococci more speedily fatal to guinea-pigs than the albumoses of either species from pure cultures.

In this connection it should not be forgotten that Nicolaier[16] as far back as 1885 observed that tetanus bacilli would multiply and produce spores in impure aërobic cultures. This very interesting effect of associated growth was later confirmed and applied by Kitasato. I have frequently noticed that in surface cultures on agar from the organs of various species of animals, anaërobes would multiply and produce perfect spores when the cultures were impure. I do not doubt that others have had similar experiences.

In these varied researches on the associated multiplication of two species in the same culture tube, or on the effect of the products of one species on another, the possibility of a permanent modification presented itself to Charrin, Sirotinin and Lorenz. Neither of the two first mentioned succeeded in demonstrating that such modification of the species under observation may and does take place. Lorenz's results are not sufficiently definite. The remaining observers were chiefly interested in watching the struggle for existence between two species or the restraining influence of bacterial products.*

I.

The incident which first attracted my attention to this subject occurred in 1890. In October of that year I made a post-mortem examination of a pig which had succumbed to hog cholera. Being

* I purposely pass over, as beyond the scope of this article, the work of those who have experimented on animals with mixed cultures. In these experiments the animal body enters as a third factor and the mutual interaction of the two species may be largely suppressed.

preoccupied with other work, I asked Dr. V. A. Moore, first assistant in the laboratory, to make cultures for me. One of these was tested on a rabbit and found to be of the usual virulence. One agar culture made directly from the liver after passing through several sub-cultures was examined by me in January of 1891. I found the culture contaminated with a liquefying bacillus which interfered with the isolation on plates. It was next passed through rabbits. One received of a bouillon culture 0.2 c.c. under the skin, the other 0.15 c.c. into the abdomen. The first did not become visibly affected. To have a rabbit survive the subcutaneous inoculation of originally virulent hog-cholera bacilli was certainly suggestive. The interest was heightened by the death of the second rabbit after nine days. The peritoneum covering the abdominal wall and the cæcum was sprinkled over with closely crowded minute whitish nodules, more or less easily teased out of their surroundings and made up of cellular elements and hog-cholera bacilli. Sections of the abdominal wall revealed collections of cells beneath the peritoneum and between adjacent muscular bundles. The centre of these foci showed extensive nuclear destruction and clumps of hog-cholera bacilli. The lesion might be aptly called a pseudo-tuberculosis. Cultures from various organs showed that the bacilli were mainly limited to these pseudo-tubercles. Cultures from this animal were re-plated and only hog-cholera bacilli found. The liquefying bacillus had been eliminated.

To confirm these unexpected results two rabbits were now inoculated from the purified culture. One received of a bouillon culture 0.2 c.c. under the skin, the other 0.1 c.c. into the abdomen. The first survived. The second died on the ninth day with the same pseudo-tuberculous lesions of the peritoneum. Even the lungs contained very minute sub-pleural nodules. There were also observed lesions more or less characteristic of certain attenuated races of hog-cholera bacilli, as they are encountered in outbreaks. These were infiltration of all the solitary and agminated follicles of the intestines, associated with necrosis of the overlying mucosa and local necrosis of mucosa of the cæcum. The spleen and liver were permeated with very minute gray foci, the mesenteric glands infiltrated, the kidneys enlarged and degenerated, the heart muscle fatty.

After a careful weighing of all the facts in the case I came to the conclusion that the liquefying bacillus was responsible for this marked modification of the virulence. I say marked, because the hog-cholera bacillus is very tenacious of its characters, and not readily susceptible to changes. An exposure of a series of bouillon cultures for 200 days at the high temperature of +3.5° C. had not yielded bacilli so attenuated as these from the mixed culture. Meanwhile the liquefying bacillus had been plated and a culture obtained from a single colony. It was subsequently indentified as *Proteus vulgaris*.

From March, 1891, until January, 1892, I kept the purified, attenuated hog-cholera bacilli growing in two series on agar; one series from the culture which had been passed through one rabbit only, the other from the same culture which had been passed through two rabbits. In January of 1892 both series were tested on rabbits, and it was found that the virulence of both had returned, for a subcutaneous dose of 0.2 c.c. of a bouillon culture was fatal in the usual time.

In order to test experimentally the attenuating action of mixed cultures four were prepared in March and April of 1891, as follows:

A. A tube of inclined agar was inoculated simultaneously from an agar culture of hog-cholera bacilli* (Virginia), and from a liquefied gelatine culture of the recently isolated *Proteus vulgaris*.

B. A tube of peptone-bouillon was inoculated in the same way.

C. A tube of agar was inoculated with hog-cholera bacilli from another source (Missouri) and with *Proteus* at the same time.

D. A tube of bouillon was inoculated simultaneously from the same cultures.

These four mixed cultures were kept after inoculation in the thermostat for several days at 37° C., then transferred to a dark chest kept cool in summer with a small quantity of ice. Every four or six weeks fresh tubes containing the same culture media were inoculated until December of 1891. It was my intention to

* This hog-cholera culture could be distinguished from the one used to inoculate *C* and *D* by its viscid colonies on agar. When this peculiarity was first noticed the culture was replated several times and passed through a rabbit, for I looked upon it as impure. The viscidity, however, maintained itself, and I was forced to acknowledge it as a peculiar feature of this hog-cholera bacillus.

examine the virulence of the cultures sooner, but other work interfered. At this late date I found a little time, and turned to these cultures grudgingly and with anticipations of wasted time. Without wearying you with the details of trying to trace the hog-cholera bacilli in these mixtures, I may state that I was unable to find any in the agar mixtures *A* and *C*. With the bouillon cultures I was more fortunate. By inoculating fresh bouillon and keeping this at 42° C. over night, I succeeded in isolating the hog-cholera bacilli from both *B* and *D* after plate cultures and the passage through rabbits had failed.

Both cultures were attenuated to a considerable degree. Subcutaneous inoculation of a much larger than the fatal dose failed to destroy, while intra-venous and intra-abdominal injections were still fatal, as the following notes prove:

Hog-cholera bacilli from mixture B:

Jan. 23, 1892. A rabbit receives subcutaneously 0.2 c.c. of a bouillon culture twenty-four hours old.

Feb. 24. The temperature taken at frequent intervals fluctuated between 102° F. and 103.6° F. The local lesion which appeared as a prominent swelling some days after the inoculation is now nearly healed.

Feb. 6. A rabbit received into abdomen 0.2 c.c. of a bouillon culture twenty-four hours old; another, 0.5 c.c. of the same culture into an ear vein. The former succumbed on the fourth, the latter on the third day.

Hog-cholera bacilli from mixture D:

Feb. 6. A rabbit receives subcutaneously 0.2 c.c. of a bouillon culture twenty-four hours old. On Feb. 11 the temperature was 106° F. From this date it gradually fell back to normal. On March 2 a dry, necrotic mass is ready to drop from the place of inoculation.

Feb. 6. One rabbit receives into peritoneal cavity 0.2 c.c. of culture used on preceding rabbit; another, the same dose into an ear vein. Both succumbed, the former in six, the latter in two days.

The objection might be raised that the pure cultures of these hog-cholera bacilli might themselves have become attenuated during this long interval of eight to nine months. This objection may be met in various ways. The pure culture of the bacillus in mixture *A* and *B* had been growing on agar during this time. A rabbit inoculated under the skin with 0.2 c.c. of a culture twenty-four hours old died in the usual time (seven days) with characteristic lesions. Again, there is no reason why bouillon cultures should

reduce the virulence more rapidly than agar cultures. As stated already, 200 days of cultivation in bouillon at 43.5° C. did not produce the degree of attenuation obtained in these mixtures. Again, I have had considerable experience during the past eight years with the hog-cholera bacillus, and have found the virulence constant for years. These culture experiments, however, simply clinch the truth of the first experiment, in which an even more pronounced attenuation had been produced on agar within the short space of three months. Why the attenuation in the later experiments was less marked than in this is probably due to a weakening of the attenuating agency itself (*Proteus vulgaris*) under prolonged cultivation or perhaps in part under the reciprocal influence of the hog-cholera bacillus in the mixed cultures.

The attenuated cultures from mixtures *B* and *D* were kept growing on agar and renewed every four or six weeks. They were used from time to time as vaccinal cultures for the immunization of rabbits. Up to October 5, 1892, these cultures served this purpose very well, for they did not prove fatal after subcutaneous inoculation. Inoculations made after this time killed the rabbits regularly. A recuperation of virulence had taken place in both cultures alike. This was not due to the passage through animals, for I had carefully kept the original purified cultures on agar only. I may state here that during the period of depressed virulence I had passed one of these cultures through four guinea-pigs successively without increasing its virulence toward rabbits. We are thus justified in assuming that the impression made upon the hog-cholera bacilli by their association with *P. vulgaris* required a certain time to become effaced, and that the animal body was, according to these results, but little more efficacious than the culture tube in restoring the *status quo*.

Before closing this part of my communication I might state that the cultivation of hog-cholera bacilli on boiled agar cultures of *P. vulgaris* for several months proved negative in reducing the virulence.

II.

The changes going on in the mixed cultures were not restricted to the hog-cholera bacilli. My attention was first called to modi-

fications of *Proteus vulgaris* in the work of isolating the hog-cholera bacillus, or rather in attempting the isolation from the mixed agar cultures, in which they were evidently no longer present. I found a variety of colonies on the gelatin plates quite different from the original colony from which they were descended. Three more or less distinct races were isolated from the agar mixture *C*. Fortunately I had preserved a pure culture of the original *Proteus* which had been growing on agar under the same conditions. It was thus possible for me to ascertain the amount or degree of change induced. This control culture likewise serves to ward off the objection likely to be raised that the races of *Proteus* were evolved simply by prolonged cultivation. Before describing them in detail a brief review of the genus *Proteus* as known in bacteriological literature will facilitate a comprehension of the results obtained

In 1885 Gustav Hauser[17] published a carefully prepared monograph on three species of a new genus created by him under the name *Proteus*. These species are *P. vulgaris*, *P. mirabilis*, and *P. Zenkeri*. Their constant habitat was meat infusion undergoing putrefaction. The growth of these species is described with minute detail by Hauser, and to his work we must refer the reader. Only a few of the fundamental characters can be given here.

In fresh gelatin cultures *P. vulgaris* appeared as a motile bacillus 1.9 to 2.5 μ long and 0.62 to 0.84 μ broad. Longer rods up to 6.25 μ in length and 0.93 μ in thickness were occasionally seen. The dimensions of the other species were about the same, with the exceptionthat they manifested a tendency toward the formation of longer segments.

A well-defined specific difference was noticed in the process of liquefaction. *P. vulgaris* liquefied gelatin quite rapidly; *P. Zenkeri* did not liquefy it at all; *P. mirabilis* stood between the two in this respect.

A character common to the three species which manifested itself on 5 per cent. but not on 10 per cent. gelatin was the power of the bacilli to swarm on the surface of the gelatin to some distance from the centre of the colony, and to produce over the invaded surface peculiar forms of secondary colonies. This same thing was observed to go on in the depths of the gelatin. The multitudinous forms of growth produced by this swarming—the appearance of

secondary and tertiary colonies—give rise to a complexity of appearances whose ensemble is readily recognizable, but whose details challenge description. Hauser was unable to give any characteristic points of difference between *P. vulgaris* and *P. mirabilis*, although he mentions certain minor differences in the appearance of the swarmed colony. Hauser's work naturally raised a number of questions, since the great range of forms found in the culture, including cocci, bacilli, spirilla, and spirulina, seemed to call forth once more the much-debated, but now apparently dead, issue of variability of the morphological characters of bacteria.

Schedtler,[18] in comparing *B. Zopfii* with cultures of *Proteus* received from Hauser, mentions *P. vulgaris* and *P. mirabilis* as liquefying 10 per cent. gelatin quite rapidly, *P. Zenkeri* as liquefying it slowly. Schedtler comes to the conclusion that Hauser's cultures were mixed with *P. Zopfii*. From my own observations I must consider this supposition unfounded.

Sanfelice[19] subsequently studied the *Proteus* forms in decomposing meat infusions. He is inclined to strike out *P. Zenkeri* and retain the two remaining species.

F. Kuhn,[20] pursuing similar studies, is inclined to drop *P. mirabilis* and retain the others.

More recently Hauser[21] himself published the statement that he had come to regard the three species described by himself as simple varieties of one species, *P. vulgaris*. He bases his position mainly on the following fact: A culture of *P. Zenkeri* which had been transferred sixty times in the course of a year to fresh media suddenly began to liquefy gelatin in a culture three weeks old. The non-liquefying form could no longer be isolated from this culture.

We will now return to the races found in the mixed cultures. Three were isolated from the agar mixture *C*. From the original control culture two slightly different races were obtained at the same time, which were included in the comparative study. In order to facilitate the description of these five races they will be denominated as follows:

1. $\begin{cases} \alpha. & \text{From the original proteus culture.} \\ \beta. & \text{From the original proteus culture.} \end{cases}$
2. $\begin{cases} \gamma. & \text{From the mixed culture } C. \\ \delta. & \text{From the mixed culture } C. \\ \varepsilon. & \text{From the mixed culture } C. \end{cases}$

The isolation was effected on gelatin plates, and great care was taken to obtain the progeny of individual bacteria by inoculating only from well-isolated colonies. They were re-plated several times subsequently. The original *Proteus*, it will be remembered, was cultivated pure since March of 1891, the varieties since February, 1892. At this time they exhibited the following differential—partly macroscopical, partly microscopical—features on gelatin plates:

α. Gelatin promptly liquefied. Colonies appear as round depressions filled with liquid, turbid gelatin. After forty-eight hours over 1 cm. in diameter. Swarming not observed. Crowded plate completely liquefied in forty-eight hours. Plate containing only twelve colonies completely liquefied in seventy-two hours.

β. Gelatin liquefied more slowly and swarming noticed, but not regularly.

α and *β* correspond closely to Hauser's *P. vulgaris* and *P. mirabilis*.

γ. Colonies show characters of preceding form *β*, with the exception that liquefaction is much more retarded. On parallel plates it appeared only after six days. In one of these colonies the following phenomena were observed on the third day:

1. A central nucleus, the original colony.

2. Within the gelatin, in a zone around this nucleus, is a large number of torula-like chains of colonies, fusiform, tapering at both ends. They are most abundant nearest the central nucleus (primary swarm).

3. Wherever the foregoing reached the gelatin surface, surface colonies have started.

4. A secondary swarm of smaller fusiform colonies around each of the primary swarms and an occasional surface colony starting from those which touch the surface.

5. Around and under the original colony and each of the primary swarms within the gelatin are zones of concentric hair-like colonies. The inclosed colony appears as if wound round and round with thread.

The whole colony including the most distant swarms is about 2 cm. in diameter.

δ. Swarming observed as with *γ*. In case of one plate fifteen original colonies completely covered the plate with primary and secondary and tertiary swarms. They differ from those of *γ* in not producing any liquefaction on the plate.

ε. Colonies show no signs of liquefaction or swarming. They appear as expansions of extremely irregular outline and have a bluish cast when viewed in transmitted light. They might be mistaken for colonies of *B. coli*.

Nearly a year later, in February of 1893, the three last mentioned varieties were again examined, this time in gelatin roll cul-

tures prepared alike. The minor differential characters are quite pronounced, as the following brief description demonstrates:

γ. In rolls, twenty-four hours old, the surface colonies appear on close scrutiny as very delicate expansions which take on more and more the form of a loose mesh-work toward the periphery of each colony, where isolated filaments appear. One colony shows swarming.

In rolls forty-eight hours old the surface colonies begin to liquefy centrally. A bristling border of radial filaments extends from the liquid into the firm gelatin.

After seventy-two hours each surface colony is 2 to 3 cm. in diameter, and liquefaction is far advanced.

δ. In rolls twenty-four hours old, the gelatin surface was covered with patches of a hazy outline and so undefined that they were at first overlooked. Some are 2 cm. in diameter. The expansion is made up of a dense network of filaments curving in various directions. Beyond this network is a zone containing a large number of isolated circles of filaments; the largest is about 0.15 mm. in diameter. Some are mere rims, others are filled up centrally, and may be likened to tubing rolled up into disk-like coils.

In rolls forty-eight hours old the entire gelatin layer is uniformly clouded by the invasion of the delicate surface growth. The gelatin appears to the naked eye as if clouded by too much alkali.

On the third day peculiar woolly spots have appeared in the gelatin which are made up of long linear threads with knobs along their course. Here and there a dense secondary swarm of very fine filaments surrounds certain places along these threads.

ε. The surface colonies appear as bluish expansions when viewed by transmitted light. The outline is very irregular and jagged. One diameter of the colony may be several times longer than the other. The deep colonies as they enlarge remain spherical.

The almost complete disappearance of the peptonizing power of varieties δ and ε is well brought out in stab cultures. Thus, after a month's growth the condition of the tube cultures was as follows in April, 1892:

α. Gelatin completely liquefied.

β. Gelatin one-half liquefied.

γ. A thin surface layer liquefied.

δ. Liquefaction barely recognizable on the surface.

ε. No indication of softening.

In another series prepared in February, 1893, the tubes were in the following condition after eighteen days:

α. One-half of gelatin liquefied.

β. One-fifth of gelatin liquefied.

$\gamma, \delta, \varepsilon$. No liquefaction yet perceptible.

In γ and δ the entire gelatin was permeated with primary and secondary swarms. In β there were some lateral root-like prolongations of the growth in the needle-track. In α and ε no swarming was indicated. This loss of the liquefying power toward gelatin was equally patent in milk cultures. While α and β caused a precipitation of the casein, showing itself on the third day and progressing toward an opalescence of the precipitate, no change was observed in tubes inoculated with γ, δ, and ε for some weeks. Subsequently, a few small floating flocculi were detected in the γ and in the δ tube when shaken, but none in the ε tube after six weeks.

This contemporaneous loss of power to liquefy gelatin and precipitate the casein in milk indicates that the two processes are due to a ferment, and that the changes produced by *P. vulgaris* in milk are not the result of an acid fermentation of the milk-sugar, as is the case in the colon group. This fact is also brought out with the fermentation tube.* In bouillon containing lactose only, no gases are set free, and the reaction of the fluid in the bulb remains alkaline. In dextrose and saccharose bouillon, on the other hand, fermentation does take place. In the culture of *Proteus* under observation, about 33 per cent. of the closed branch became occupied with gas. The gas accumulated slowly, and no increase was observed after the tenth or twelfth day. If we regard the explosive residue left after removing the CO_2 with KHO, as hydrogen, the fraction $\frac{H}{CO_2}$ equals for dextrose $\frac{5}{2}$, for saccharose $\frac{5}{3}$ approximately. In both sugar solutions the reaction became markedly acid.

It is of interest to note that while the peptonizing power of the *Proteus* varieties had largely disappeared, the fermentative character remained unchanged. There was no difference whatever between α and ε in bouillon containing dextrose, saccharose, and lactose as regards the quantity and quality of the gases set free and the reaction of the fluid. The fermentation tube would thus furnish a

* The Wilder Quarter-Century Book, 1893, p. 187.

prompt, unmistakable means of differentiation between *Proteus* ε, the non-liquefying variety, and the colon group.*

The morphology of these artificial varieties still claims our attention. The following notes refer to cultures in the same bouillon, made at the same time, and forty-eight hours old:

α. Mostly short bacilli, about 1.2 μ long and 0.6 μ broad. A few are 2 μ long. There are also some filaments up to 20 μ long, some slightly wavy.

β. Does not differ from α excepting in the additional presence of a moderate number of deeply stained straight rods, single or in pairs, about 4 μ long.

γ. A considerable number of very long filaments stretching nearly across the field, some jointed, others not. Some are wavy. Some are thick and deeply stained, others appear as degenerated hollow tubes feebly stained on the borders. There are also present some small, thin, regularly segmented filaments.

δ. Resembles γ in the great variety of forms present. The filaments are in general shorter and more vigorous in appearance. A few are wavy. There are also a few slightly curved forms simulating comma bacilli.

ε. The morphology of this culture stands nearest to α in the regularity of forms and the scarcity of long filaments. The bacilli appear distinctly larger than those of α, the shorter being 1.8 to 2 μ long, and perhaps 0.1 to 0.2 μ broader than those of α.

The changes thus briefly sketched must be largely ascribed to the partial or complete loss of capacity to secrete a peptonizing ferment. This loss determines the appearance of the colonies, and may lead to the production of involution forms on account of the changed life to which the bacilli are subjected in unliquefied gelatin. A change of function may thus influence form. The power to swarm seems to grow with a certain diminution of the liquefying capacity and then to disappear with the latter completely. This peculiar property of swarming deserves a careful investigation, and I pass over here any discussion concerning it.

The genus *Proteus* is too important a species to be neglected by pathologists, and the question arises what shall be done with the classification proposed by Hauser. It is more than probable that

* Of the five varieties three have been kept growing on gelatin up to the present (May 30, 1894). These are α and β of the original culture, and ε of the mixed culture. α still liquefies promptly, while β has lost this power, though still swarming. ε has not changed during the past year. The fermentative power of the least and that of the most changed variety remain practically the same, thus indicating a remarkable tenacity of these fundamental characters. It should be stated that an increase of or a return to the peptonizing power, as was observed by Hauser, has not occurred in any of my cultures.

we have to do here with a bacillus undergoing variation more promptly and transmitting such variations more readily than any other form hitherto carefully studied. There can be no question that *P. mirabilis* is *P. vulgaris* with reduced peptonizing powers, and is readily identified with race γ. According to Hauser's original description of *P. Zenkeri*, race ε agrees closely with it, since neither swarms nor liquefies gelatin. On the other hand, a culture of *P. Zenkeri* obtained from Kral grew in a manner quite different from that described by Hauser. In rolls of 10 per cent. gelatin there appear within twenty-four hours, dry, delicate surface colonies, which finally attain a diameter of 1 cm. Under a low power these are resolved into a remarkable configuration of S-shaped patches of bacilli connected with one another by strands of filaments. The depths of the gelatin are penetrated by long, straight, linear growths, more or less torula-like and resembling somewhat the delicate secondary swarms of *P. mirabilis*. In bouillon the bacilli are motile and broader and longer than those of the other species. Involution forms and long filaments are absent. Kuhn likewise describes *P. Zenkeri* as a delicate, fungus-like growth in 10 per cent. gelatin. This form would thus agree most clearly with my variety δ. Unfortunately the culture disappeared from my collection before its fermentative action on different sugars had been tested.

In view of this confused state of affairs, I would suggest that in the study of doubtful forms we should apply the fermentation test, and class those species which fail to act on lactose, but which ferment dextrose and saccharose as described above under *Proteus*. I found the fermentation test such a valuable group reaction, that I can safely recommend it in the study of all saprophytic forms in supplying a broader view of the relationship of physiological species.

III.

Before endeavoring to trace the immediate practical bearing of the results obtained, let us briefly note what they really are.

A pathogenic bacillus of a refractory nature, by accidental symbiosis with *Proteus vulgaris* was promptly reduced in virulence so as to produce in rabbits a modified, prolonged inoculation disease characterized by an eruption of pseudo tubercles and typhoid-like lesions

of the digestive tract. In a repetition of this experiment two hog-cholera cultures obtained from different States were attenuated in symbiotic growth with *P. vulgaris*. The period of association lasted about nine months; that of reduced virulence in pure cultures about the same length of time. *Proteus vulgaris* underwent changes in the mixed cultures much more rapidly than in pure cultures. Several varieties were isolated, all originally derived from a single colony. These manifested reduced and lost peptonizing powers and slight morphological differences. They agreed closely with the forms originally described by Hauser as three separate species.

The most interesting feature of these observations, at least the one which surprised me most at the time, was the return of the hog-cholera bacilli in every case to a higher plane of virulence after the prolonged stay at a lower level. This fact suggests a certain degree of inertia in recovering pathogenic powers, as well as a remarkable tenacity of those powers. The attenuation in mixed cultures is evidently due to forces quite different from those at work in ordinary pure cultures, in which a gradual loss of virulence almost invariably manifests itself after years of cultivation. From these observations we may further deduce, if not a demonstrated fact, at least a suggestive thought. They show, I think, that bacteria may be influenced and modified when not actively multiplying. The whole trend of thought on the modification of bacteria seems to have been that the changes are most surely and promptly produced if the bacteria under the immediate influence of modifying forces can be made to go through the greatest number of generations. This conception is not supported by the culture experiments described. Cultures of hog-cholera bacilli are, as a rule, full-grown in three or four days, and multiplication probably goes on very slowly thereafter. Yet the influence exerted by *Proteus* must have been continuous, for I believe it impossible to modify the hog-cholera bacillus in eight or nine consecutive subcultures of three or four days each. The influence was actually at work in eight or nine subcultures, each lasting about four weeks, in which only a trifling change or none at all could be noticed after the first few days.

Another fact deducible from these culture series which may occasion surprise is the persistent vitality of the hog-cholera bacilli during a long intimate association with a vigorous saprophyte.

The experiments of others have shown a more or less rapid destruction of pathogenic forms in mixed cultures. Thus, Vincent states that in mixed bouillon cultures of *P. vulgaris* and the typhoid bacillus at 37.5° C., the latter disappeared in sixty hours. The typhoid and the hog-cholera bacillus are so closely related that the statement of Vincent seems to me to need confirmation. Evidently the insufficiency of methods in disclosing the presence of a few bacteria of one kind among a large number of another kind is mainly responsible for the views hitherto held concerning the active destruction of one species by another. When a number of species vegetate together, the disappearance of one species is probably due to a combination of several factors, such as inhibition due to insufficient food and the presence of acid products which are almost equally destructive to the species producing them. Other factors independent of bacterial life, such as absence of oxygen, the presence of sunlight, etc., may enter. One of the important bacteriological problems of the future will be the detection of a residuum of pathogenic bacteria surviving in the midst of saprophytes.

Perhaps the most important thought suggested by the subtle influence which one species of bacteria may exert upon another is the possible elevation of the pathogenic power of bacteria. Stated in another more concrete form, the problem is this: If the hog-cholera bacillus can be markedly and rapidly changed when growing with *Proteus*, may not the nature of *Proteus* be changed so as to approach that of the hog-cholera bacillus? I have already referred to the conversion of the pseudo-œdema bacillus into a temporary tetanus bacillus by Sanfelice.[12] This author also changed the non-virulent form of the *Rauschbrand* bacillus into a virulent form by cultivating the former in boiled tetanus cultures. Unfortunately, my own observations were not followed out in this direction, and they simply give a hint. The possible change in the nature of *Proteus* is suggested by the following inoculation experiment:

One of the mixed bouillon cultures, after nine months' growth, was passed through a rabbit for the purpose of eliminating, if possible, the *Proteus*. A fresh tube of bouillon was inoculated from it, and three days later 0.5 c.c. of this injected into the ear vein of the rabbit. On the ninth day, after apparent recovery, it had convulsions and was chloroformed.

The spleen was found slightly engorged, the kidneys far advanced in

degenerative changes. Follicles in the appendix vermiformis and Peyer's patches near the valve somewhat conspicuous. The most peculiar changes were found in the skeletal muscles of the entire body with the exception of the head. Slender, whitish, fusiform lines, closely simulating sarcosporidia cysts, were imbedded in the muscles. They were about 1 cm. long and up to 0.5 mm. in diameter. Examined fresh, in teased and crushed preparations, they were found to be necrotic fibres intermingled and surrounded by fibres undergoing fatty metamorphosis. In sections of hardened tissue more or less cell infiltration and proliferation was noticed around these necrotic foci which involved from a few to ten fibres. The age of these lesions was evidently not greater than that of the inoculation disease. *Proteus vulgaris* was demonstrated in cultures from the liver, spleen, and blood, but not in cultures from the affected muscular tissue. Hog-cholera bacilli were not detected. They were, however, subsequently isolated from the mixed culture directly.

I am inclined to think that the muscular necroses were the work of *Proteus* and that this unusual localization was due to a modification of the latter toward what we may fitly consider a higher pathogenic level. Unfortunately, a single instance cannot be regarded as demonstrative in bacteriology, and the proof is unsatisfactory. I need not, however, insist on the importance of this problem of studying any interchange of characters of bacteria in mixed cultures. The subtle influence of such associated growth is evidently superior to that of all other processes hitherto employed in the modification of bacteria. A little reflection will convince us of the naturalness of this fact. We have been impressed with the remarkable immunizing potency of the blood-serum under certain conditions, and we have been surprised by its equally remarkable bactericide powers. Slowly we are coming to learn that the more subtle influence is exerted by biological, rather than by physical and chemical forces, and that in the action of like or related energies upon one another the solution of many difficult problems in biology and medicine will be found.*

The foregoing deductions and inferences are presented with some hesitation. In endeavoring to apply them to the more practical problems of hygiene the hesitation increases, for they have as yet little to support them. There prevails to-day a strong tendency,

* I have purposely omitted any reference to the well-established method of increasing the virulence of bacteria by passing them through a series of animals. The hypothesis that bacteria may temporarily acquire disease-producing powers by associating with one another is suggested as one of perhaps many factors in the evolution of disease germs.

for good or for ill, to withhold hypotheses until their presentation can be accompanied by demonstration, such as it frequently is. I cannot refrain from agreeing with P. Ehrlich, however, when he states* that progress in knowledge or insight can take place only from a theoretical point of view, and that even a missed theory may be more fruitful than crude empiricism which records the fact without an attempt at interpretation.

The most important hypothetical application of the facts obtained from the mixed-culture experiment is to the processes going on in the superficial layers of the soil, and more particularly the soil polluted with excrementitious matter. We may conceive such a soil containing pathogenic, putrefactive, and ordinary saprophytic bacteria, multiplying to a certain degree perhaps, and influenced by concentrated bacterial products evolved in the soil and leached out by the water from the excrementitious matter. The intermingling of living bacteria must likewise be a potent factor in the modifications of these organisms. If it is possible that bacteria may be modified when not actively multiplying, and if bacteria may acquire invasive properties in the soil under the conditions cited, it is not difficult to understand how epidemics and epizootics may appear and, after prevailing for a time, again disappear. The pathogenic powers temporarily acquired in the soil would be lost after a time in the human or animal body, and the resulting disease would thus be self-limited. All that is necessary for such a hypothetical epidemic to develop is the bringing together of the disease germ, perhaps largely in polluted water, with the susceptible body. The selective absorption of the latter results in forming the primary focus of disease. If we assume the modification of bacteria by bacteria in the soil, the much-debated hypothesis of Pettenkofer concerning the influence of season and locality on disease would perhaps appear to bacteriologists in a much more acceptable aspect.

This hypothesis I would not apply to well-established pathogenic bacteria, for they obviously must seek their further advancement as specific disease germs in a more complete adaptation to their host. It may, however, account for the occasional springing up of infectious diseases whose etiology is involved in obscurity, such as

* Das Sauerstoffbedürfniss des Organismus, 1885, p. 105.

diarrhœal and dysenteric diseases, or those whose appearance is governed by unknown factors, such as Asiatic cholera. The recent isolation from water of a number of comma bacilli not satisfactorily differentiated from the true organism lends color to this hypothesis.

In conclusion, I wish to call attention briefly to the possible application of mixed cultures in the investigation of purely pathological problems. The suitable modification of pathogenic bacteria should enable us to study to more advantage the mutual action of pathogenic species and the animal body on each other. We should be able to obtain by properly grading the virulence what mathematicians might call the consecutive states of pathogenic activity, from which the "differential coefficient" or the true *modus operandi* of each species may be derived.* Such studies would contribute much toward harmonizing many of the conflicting views on questions pertaining to the production of immunity. Experiments in the hands of one may fail, while in the hands of another they may succeed because a less virulent race of bacteria has been used. Both experimenters may be right, but they are working on different portions of the same complex curve. Undoubtedly much of the discord concerning the immunizing and curative action of tuberculin on rabbits and guinea-pigs is due to this or some allied cause. Every other pathogenic species has been the object of similar but less conspicuous controversies.

To reduce or perhaps increase the virulence of bacteria in mixed cultures will undoubtedly meet with many obstacles in practice. The more delicate, perishable species may refuse to multiply in company with others, and it may require much labor to find the species with which they will continue to thrive. Perhaps the use of filtered cultures may solve this difficulty, provided the modifying forces are not linked indissolubly to the presence of the living bacteria themselves. In any case prolonged cultivation may be necessary to induce modification, and for this an extra supply of patience will be useful in these days of hurried work and still more precipitate publication.

* An attempt of this kind has been made by the writer in conjunction with Dr. V. A. Moore in the study of certain infectious animal diseases. See Bulletin No. 6 of the Bureau of Animal Industry of the Department of Agriculture (1894), p. 81.

INDEX TO ARTICLES REFERRED TO IN THE TEXT.

1. *Charrin:* La Maladie pyocyanique, 1889, p. 111.
2. *Blagovestchensky:* "Sur l'Antagonisme entre les Bacilles du Charbon et du Pus bleu." Annal. de l'Inst. Pasteur, 1890, p. 689.
3. *Vincent:* Compt. rend. Soc. de Biol., 1892, p. 597.
4. *d'Arsonval et Charrin:* "Action des Microbes pathogènes sur la Cellule végétale." Ibid., 1893, p. 37.
5. *Mühsam and Schimmelbusch:* "Ueber die Farbstoff-produktion des Bacillus pyocyaneus bei der Symbiose mit anderen Mikro-organismen." Archiv f. klin. Chirurgie, xlvi., S. 677.
6. *Vincent, H.:* "Sur les resultats de l'Association du Streptocoque et du Bacille typhique chez l'Homme et les Animaux." Annal. de l'Inst. Pasteur, 1893, p. 141.
7. *Salkowski, E.:* "Bemerkung zu der Mittheilung von M. Nencki: Ueber Mischkulturen." Centralbl. f. d. med. Wissenschaften, 1892, xxx., p. 305.
8. *Garré:* "Ueber Antagonismus unter den Bakterien." Deutsche med. Wochenschrift, 1887, S. 597.
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12. *Sanfelice, F.:* "Untersuchungen über anaërobe Mikro-organismen." Zeitschrift f. Hygiene, 1893, xiv., pp. 339-393.
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14. *Nencki:* "Ueber Mischkulturen." Centralblatt f. Bakteriologie, 1892, xi., S. 225.
15. *Von Schreider:* "Uber Mischkulturen von Streptokokken u. den Diphtherie-bacillen." Centralblatt f. Bakteriologie, 1892, xii., S. 289.
16. *Nicolaier:* Quoted in Flügge's "Die Mikro-organismen."
17. *Hauser, G.:* Ueber Fäulnissbakterien und deren Beziehungen zur Septicämie. Leipzig, 1885.
18. *Schedtler:* "Beitrag zur Morphologie der Bakterien." Archiv f. pathol. Anatomie, cviii., p. 30.
19. *Sanfelice, Fr.:* "Contributo alla Biologia e Morfologia del Batterie saprogeni aërobi e anaërobi." Atti della Accademia Med. di Roma, Serie 2, vol. v.
20. *Kuhn, F.:* "Morphologische Beiträge zur Leichenfäulniss." Archiv f. Hygiene, 1891, xiii., S. 40.
21. *Hauser, G.:* "Ueber das Vorkommen von Proteus vulgaris bei einer jauchig-phlegmonösen Eiterung nebst einigen Bemerkungen zur Biologie des Proteus." Münchener med. Wochenschrift, 1892, p. 103.

DISCUSSION.

DR. G. M. STERNBERG: This paper of Dr. Smith's is very interesting, and deals with a line of research that is quite instructive. A few years ago our bacteriologists were disposed to look upon cultures which showed small differences as being of different species. I think that the teaching in Koch's laboratory and in other laboratories of Europe not many years ago led to that idea, and our bacteriologists, following that teaching, when they found that a particular bacillus, although in many respects it seemed exactly like another, yet produced a little more acid, as shown in litmus-milk culture,

concluded that it was a different organism. I know that my friend Dr. Booker, in Dr. Welch's laboratory, in working over the various bacteria which he got from the intestinal discharges of children with cholera infantum, got out a great number of bacteria which resembled each other very closely, and he evidently was very much confused, as many others have been since, as to whether he had different species or only different varieties of the colon bacillus. We know now that there are many different varieties of the colon bacillus, and that this bacillus, like the typhoid bacillus and others, undergoes various modifications. Liquefying organisms may fail to liquefy; phosphorescent bacteria after a time may fail to produce phosphorescence, and the pigment bacteria may fail to produce their pigment. Starting with pure cultures from the same source, we can get a large number of varieties. It is a question still to be decided whether any of these varieties have permanent characters and fail to return to the original type.

In regard to the colon bacillus, I went through this whole thing in my investigations in Cuba, and was very much perplexed by finding that when I started from a single colony obtained from the intestine of a yellow-fever case and got what appeared to be the colon bacillus in one case, and then started from a second colony which seemed to be quite different, I subsequently got identical colonies. I was led from the very peculiar colonies in one instance to think that I had discovered something that was new. Bringing back my cultures and working over them in the laboratory in Baltimore I found that I no longer got the peculiar rosette colonies found in Havana, but typical colonies of the colon bacillus. Having in several instances, in cultures of the colon bacillus made from a simple colony, discovered a branching growth that looked as if it was something entirely different, I broke the tubes and inoculated a new culture from the branching growth; from this I obtained a growth that was quite different from that of the colon bacillus in gelatin stick cultures. But testing the thing over and over again, I found that it was a pure culture like the single colony I started from. In this branching outgrowth the bacilli were longer than in other portions of the culture. It was doubtless a "sport," very much perhaps as we have in the higher plants. In a geranium, for instance, propagated by slips year after year, suddenly you may find a sport—the leaves have different shading, or a different shape, and this sport is cultivated and propagated. In the same way we seem to have sports among these low plants. We have gradual changes as the result of conditions of growth, and we may have the more sudden change I speak of, as in this outgrowth from the colon bacillus.

One point referred to by Dr. Smith in his paper reminded me of Dr. Ernst's paper read yesterday. This point, which I did not think of yesterday, has reference to the pathogenic power of a pseudo-tetanus bacillus which had been cultivated in the soil where the tetanus bacillus had previously been cultivated, and after being propagated through successive tubes, still killed animals with all the symptoms of tetanus. Now that corresponds

very well with what Dr. Martin had in his inoculations with a particular bacillus obtained from vaccine lymph. After several generations this bacillus still produced a typical vaccine vesicle. Whether his bacillus would continue to do so indefinitely is a matter to be determined by further experiment. The tetanus bacillus produces a most potent toxalbumin, and whether the pseudo-tetanus bacillus somehow manages to carry this with it, or whether it acquires the property of reproducing this toxalbumin, or what the explanation may be, I am not prepared to say; but the fact is as stated, and it seems to me a parallel case to that of the bacillus cultivated from vaccine vesicles. I think it is in this line that investigation should be carried on with reference to the results reported by Dr. Martin.

Dr. W. H. Welch: Regarding the question discussed by Dr. Sternberg as to the relation of the changes described by Dr. Smith to the production of distinct bacterial species, it seems to me that it is well to bear in mind that nearly all of these artificial modifications produced by the action of different agencies on bacterial cultures are changes in function and not morphological changes, and that the present tendency among biologists is to eliminate, so far as possible, in the classification of species, physiological properties, so that it seems to me that in these observations there is nothing that necessitates our supposing that these changes justify the recognition of anything more than races and varieties, and not of separate species.

I quite agree with Dr. Smith as to the remarkable tenacity of the hog-cholera bacillus in its pathogenic properties. It is extremely difficult to modify them. This is directly contrary to the statements of Selander and of Metchnikoff. I think it should be proclaimed that the hog cholera bacillus which they are working with at present is not our American hog-cholera bacillus. It is quite evident to all of us here that Metchnikoff is certainly working with some different organism. We have gone over the original experiments of Selander, who claimed to increase the virulence of the hog-cholera bacillus so that it became a germ almost identical with that of ordinary rabbit septicæmia, that would kill in twelve to eighteen hours. We have gone over that work repeatedly, and have not been able to secure the same results. There must have crept into this somewhat rather rough experiment of crushing the spleen, a bacillus that belonged to the group of rabbit septicæmia, and they have gone on working with the rabbit septicæmia ever since.

Regarding these lesions in the intestines of rabbits which Dr. Smith attributes to the attenuated bacillus, we have found these same lesions occasionally after inoculations with the ordinary hog-cholera bacillus.

Of course all of this bears directly upon our conception of the way in which bacteria are associated in the outer world. They do not exist there in pure cultures. Dr. Smith has worked with one of the most widely prevalent organisms of the outer world—the ordinary proteus—which occurs frequently in decomposing substances, and this organism seems to modify

the properties of other pathogenic bacteria. It attenuated the hog-cholera bacillus in his cultures, and it is well known that it modifies the properties of the micrococcus lanceolatus, and of the typhoid bacillus, or of the susceptibility to these organisms. These bacteria are associated in various ways in the outer world, and they are capable of attenuating or exalting or modifying in different ways the properties of pathogenic bacteria, and although we have not very definite information as to the exact conditions existing outside, yet these results are very suggestive to my mind that the conclusions that we draw from experimenting with pure cultures are not exactly applicable to the real conditions as they exist in Nature.

Dr. Theobald Smith: Just one word more. In regard to the typhoid-like lesions produced by hog cholera, I may say that I studied them in various ways, and have come to the conclusion that they can be produced in two ways—either by an attenuation of the germ, or by increase of the resistance of the animal. The definite relation which exists between a virulent hog-cholera germ and a vaccinated rabbit is identical with that existing between an attenuated hog-cholera germ and a normal and not vaccinated animal. These two lines of investigation converge to the inference that these intestinal lesions, which are always associated with the prolonged life of the rabbit, are due to one or the other of these causes.

Regarding the work of Selander and Metchnikoff, I may state that there is now a bulletin in press to be issued by the United States Agricultural Department which goes into this subject fully.

NOTES ON THE OBSERVATIONS OF MALARIAL ORGANISMS IN CONNECTION WITH ENTERIC FEVER.

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THE possibility of typhoid and malarial fever manifesting their symptoms at one time in the same individual has afforded a fertile subject for debate for many years, with the result that the belief in the simultaneous action of the two infections has been gradually losing advocates. The theory originally advanced by Woodward, that a "typho-malarial fever" exists as a specific and independent disease, other than a typhoid fever made irregular by admixture with malarial poison, has been more and more abandoned by competent clinicians, as it subsequently was by Woodward himself, although it is occasionally revived in the South and Southwest in discussions upon the continued fevers of the South, especially in newly settled localities whose success as health resorts is closely connected with a belief in the entire absence of typhoid fever.

An exceedingly interesting paper was read before this Association six years ago by Dr. Johnston,[1] in which he summarized data in regard to the relation of typhoid fever to fevers of malarial origin, based upon replies to questions sent to 350 physicians residing along our Atlantic and Gulf seaboards. Dr. Johnston's contribution to this subject is familiar to us all, but I desire to refer briefly to one or two of its features. The research elucidated very strikingly the variations in type of enteric fever depending upon locality.

[1] "On the Geographical Distribution of Typhoid Fever in the United States; its Relation to Fevers of Malarial Origin," etc. By W. W. Johnston: Trans. Assoc. Amer. Phys., 1888, vol. iii. p. 8.

Two of the questions propounded were the following:

1. "Do you recognize in your practice a distinct type of continued fever which is neither malarial nor typhoid, or one which is a compound of both—a typho-malarial fever?"

2. "Do you think that the typhoid fever which you see is modified by malarial infection?"

The answers to the first question conform to geological distribution, the existence of a "typho-malarial fever" being very generally denied in the Northeastern States, and affirmed by rather more than one-half the answers received from Eastern North Carolina, South Carolina, Georgia, and Florida.

In answer to the second question, some stated their belief that in certain localities in the South "all the forms of fever seem to be more or less complicated with malaria, so much so that it is almost impossible to treat it successfully without the use of quinine in considerable quantities." Others living further to the northeast affirmed that "there are no mixed continued fevers."

The belief is, I think, almost universal that typhoid fever, as observed in New York, is uncomplicated by malarial infection, and that quinine, except as a tonic in convalescence, is worse than useless in its treatment. For this reason the following cases, seen in New York last summer and autumn, are of unusual interest.

Case I.—The patient, J. McN., male, a native of the United States, forty-three years of age, was admitted to the Presbyterian Hospital, New York, on August 18, 1893. He denied having had ague, and gave no previous history of interest except that for the past twelve years he had indulged at intervals in the opium-habit, taking of late as much as twenty grains per diem. For three days he had been ill with headache, vertigo, prostration, epistaxis, and slight cough, with mucous expectoration.

On admission, his appearance suggested typhoid fever, and he was treated accordingly by the Brand method of cold tub-bathing. There were slight enlargement of the splenic area of dulness, great prostration, diarrhœa, and a typical typhoid tongue—dry, coated on the dorsum with thin red margins and swollen papillæ. There was continued fever, which lasted for seven weeks, and during this period the patient developed the following symptoms: a genuine typhoid eruption, there being some forty distinct rose spots on the abdomen and chest, which appeared in successive crops; hemorrhages from the bowels, of which there were four or five of considerable amount, tympanites, bronchial catarrh, slight albuminuria with granular casts, semi-stupor and delirium, subsultus, great prostration and emaciation, and the facies of the typhoid condition.

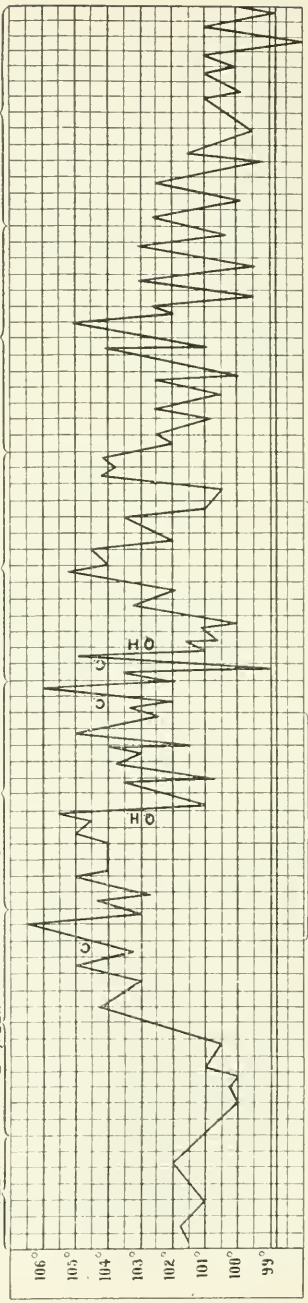

1ST WEEK
2D WEEK
3D WEEK
4TH WEEK
5TH WEEK
6TH WEEK
106°
105°
104°
103°
102°
101°
100°
99°
H
O
Hemorrhage from bowels.
Very abundant malarial organisms.

CHART I.

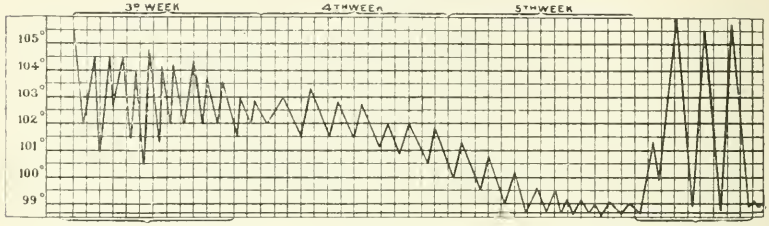
On the thirteenth day of the illness there was a severe chill, lasting about three-quarters of an hour, and so violent that the patient shook the bed. It was accompanied by a rise of temperature to 106.6° F., but there was no sweating. During the third week two other chills occurred of equal violence. As the first chill took place before the hemorrhage, and also before the eruption became decisive, and as there was nowhere evidence of suppuration, it appeared possible that there might be an error in the diagnosis, and the blood was carefully examined for the malarial plasmodium. It was found in exceptionally large numbers invading the red blood-corpuscles and also independent of them. When the next chill and exacerbation of temperature occurred quinine was given hypodermatically with the effect of reducing the temperature 4.5° (105.5 to 101° F.). This treatment was several times repeated, and on one occasion, at the end of the third week, the temperature was temporarily reduced from 106.4° to 99° F. No more chills occurred after the beginning of the fourth week, but the use of quinine was continued by the mouth, and the bathing, previously interrupted by the hemorrhages, was resumed. The patient made a good recovery, and after fifty-five days in the hospital was discharged, cured.

I regret that no examination of the stools for typhoid bacilli was made, but in view of the distinct eruption, epistaxis, intestinal hemorrhages, and tympanites, in connection with all the other symptoms, there can be no reasonable doubt that typhoid fever was present, and repeated examinations of the blood proved the presence of the malarial organisms on each occasion. (There was nothing in the character of the stools to indicate dysentery.) I have never seen a more complete picture of enteric fever as regards all the symptoms, excepting the chills and irregular temperature curve.

Case II.—The patient, J. J., an Irish laborer, thirty years old, was admitted to the New York Hospital on July 25, 1893. Two weeks before admission to the hospital he had had five or six chills of considerable severity, accompanied by nausea, vomiting, slight diarrhœa, and fever. He had complained also of severe frontal headache. On admission, the spleen could be palpated half an inch below the free border of the ribs, and two or three dozen rose spots were found upon the chest, abdomen, and back. The Ehrlich reaction was present. There were tympanites and slight albuminuria, with decided prostration. The tongue was dry, coated on the dorsum, with thin red margins and prominent papillæ. The patient was treated by cold tub-bathing without medicine. He received in all thirty baths. The fever ran as typical a typhoid course as one often finds when cold "tubbing" is employed; the maximum temperature was 104.5° F., and it became normal upon the thirty-first day. The Ehrlich reaction disappeared. The temperature remained below 99.4° F. for several days, and on the thirty-

seventh day suddenly rose to 106° F., and was accompanied by profuse perspiration. There were chills and high fever (105.5° F.) on each of the two successive days at the same hour, and Dr. Ferguson, the pathologist of

CHART II.



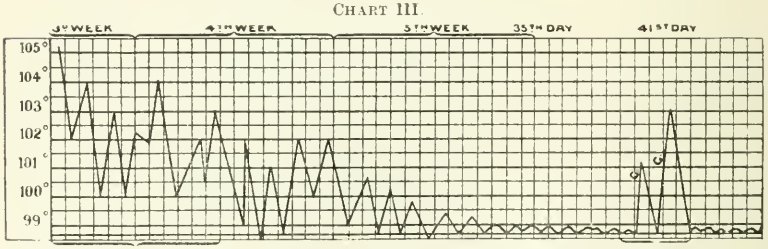
Cold tub-baths. Abundant malarial organisms.

the hospital, who examined the blood for me, found malarial organisms in abundance in the blood. From the continued giving of quinine the patient had no more chills or fever, and in a few days he was discharged, cured.

There can be no question that this was genuine typhoid fever. The course and duration of the fever, the headache, diarrhœa, enlarged spleen, the appearance of the tongue, the facies and hebetude of the patient, and the distinct rose spots, all combined to make the case typical. The following case is very similar to the preceding:

CASE III.—The patient, W. L., male, United States, a laborer, twenty-seven years old, was received at the New York Hospital on the nineteenth day of his illness. His temperature then was 104.5° F.; respiration, 24;

CHART III.



Cold tub-baths. *Pigment* found in blood corpuscles, but no germs.

pulse, 100. There was a distinct eruption of rose spots on the abdomen and thorax, a red, dry tongue with swollen papillæ at the tip, great prostration, and the facies of enteric fever. The spleen was palpated half an inch below the free border of the ribs. The patient was treated by cold tub-bathing,

receiving twenty-one baths in all. He made a good recovery, and after ten days of normal temperature he was allowed the freedom of the ward. He was about to be discharged as cured on the forty-first day, when he had a severe chill, lasting half an hour, followed by fever and sweating. The chill was repeated the next afternoon at about the same time, also with increased temperature. Quinine was promptly given and the blood was not examined until the patient had received twenty grains. No malarial organisms were then found, but abundant malarial pigment granules were contained in the blood cells. Under the continued use of quinine, the patient recovered three days later.

In the first case reported the plasmodium became active during the height of the typhoid disease. In the second and third cases the malarial symptoms remained latent (although the plasmodium must have been already present) until the force of the enteric infection had been completely expended, when they assailed a body weakened by a fever of considerable duration. This is of interest in view of the well-known fact that in those who are subject to malarial paroxysms the malarial poison often takes advantage of lowered conditions of the system produced by fatigue, exposure, inanition, constipation, etc. It may be noted that neither of these patients recalled having had previous attacks of ague. With regard to the first case, it is to be observed that the typhoid fever, at first very mild, was immediately greatly aggravated by the malarial complication. The patient's condition was so reduced by it that his death seemed imminent. The sudden reductions in temperature which took place bore a definite relation to the giving of quinine, and not to the hemorrhages. The chills also were not connected with the hemorrhages.

The advocates of typho-malarial fever as a distinct disease usually emphasize the absence of rose spots as invariable.[1] Others, who deny the possibility of the coexistence of malarial and enteric fever, account in various ways for the chills and sweating in cases presenting a similar clinical picture to those above reported, they not having found the malarial plasmodium in the blood. Thus, Bouveret[2] reports four such cases in which he believed the modified symptoms were due to a slow and irregular elimination of toxic material, a large volume of which is sometimes thrown into the blood at once;

[1] Squire: Epidemiol. Soc. of London. Lancet, January 8, 1887, p. 73.
[2] Lyon Médical, June 5 and 12, 1892.

and Fränkel[1] reports a similar case in which he thought the symptoms might be due to a thrombus in a mesenteric vessel, with suppuration and possibly miliary abscesses in the liver.

Prof. Osler, in a recent number of the *Johns Hopkins Hospital Reports* (vol. iv., No. 1), mentions three interesting cases in which malarial fever was present with the plasmodium within a few months of the occurrence of enteric fever, and once within a few days, but as the result of his experience he says: "There was no case with the characters of the two diseases so blended that it seemed a compound or hybrid malady, nor was there an instance in which the manifestations of the two diseases were concurrent."

It is not well to draw hasty conclusions from a very limited number of cases, but there is a kind of evidence which does not need to be multiplied to be convincing; and it seems to me, from the observations of the few cases herewith presented, that while it is unwise to accept the term typho-malarial fever as indicating a third form of disease, which is neither typhoid fever nor malarial fever, it cannot be denied that the two latter diseases may coexist. Case I. certainly proves that they may do so, and this in a part of the country in which this form of double infection is most unlooked for, and the other cases, although perhaps less striking, are at least corroborative.

DISCUSSION.

Dr. Wm. Osler: The first case of Dr. Thompson's is of unusual interest. I know of no instance in the literature in which the two diseases have been so accurately and carefully described running concurrently. It would be a very great mistake to suppose that chills in typhoid fever always indicate malaria, since it is well recognized that they are by no means uncommon, and due to various causes. Within the past year at the Johns Hopkins Hospital we have had several instances of typhoid fever with heavy chills, in which the malarial parasites were not present. I show here a chart of the only case in which the patient was admitted to the hospital with a double infection of malaria and typhoid fever. The man, aged twenty, had for sixteen days prior to admission, headache, cough, occasional nose-bleeding, and three chills. On admission, October 16th, the temperature was 100°, but fell

[1] Ibid., June 19, 1892.

in the early morning of the 17th to 96°. The malarial parasites were found to be present in the blood. He was ordered quinine, four grains, three times a day. On the 17th the temperature began to rise a little after 12 M., and at 3.30 P.M. he had a chill, after which the temperature rose to nearly 105°, then fell throughout the next night, and was normal at 8 A.M. The case was one of ordinary tertian intermittent, and the quinine was continued. On the 18th, 19th, 20th, 21st, and 22d, the temperature was normal or subnormal. A two-hourly temperature had been taken. Up to 8 A.M. on the 22d he had taken eighty grains of quinine. He had no more fever, and the malarial parasites had disappeared from the blood. At 8 A.M. on the 22d the temperature was 97.5°. At 4 P.M. it was 98°. It gradually rose through the evening, and at 12 midnight it was 102.5°. The next morning it was 102.2°; rose throughout the day, and from 4 to 8 P.M. was at 105°; so that within the twenty-four hours from 4 P.M. of the 22d to 4 P.M. on the 23d, the temperature had risen 7°. This rise was the beginning of a very severe attack of typhoid fever, with all the characteristic features of the disease, the temperature not reaching normal until the sixth week, and during it he had not a single feature pointing to any influence of malaria.

We have recently had under observation an instance in which malaria and pneumonia were concurrent; a very interesting case, indeed, of which I will pass around the temperature chart The man came in on the third day of his illness, temperature 102°, with the history of chills a year previously, and residence in a very malarial district. In the house in which he had been living, near Sparrows Point, the woman and her three children had suffered from malaria. His illness began two days before admission, and we regarded the case at first as probably typhoid fever. The blood, examined on admission, was negative. On the third day of the fever the malarial bodies were present in numbers. He was then given quinine, five grains in every four hours; and you will notice by the chart that the temperature went along uninfluenced by the quinine at all, although the malarial parasites disappeared from his blood. He had a very severe attack of pneumonia; had sweats on one or two days; no chills. On the eleventh day the crisis occurred, not very abruptly, and he entered upon a very satisfactory convalescence. Quinine was kept up from the seventeenth to the twenty-first. The blood was repeatedly examined, and the parasites were absent. Then it is interesting to note that just before he left the hospital, and nearly three or four weeks following his apyrexia, he had two chills and malarial organisms were demonstrated in the blood, so that the quinine which he had taken during the fever had not entirely destroyed the parasites. In all probability his malarial infection dates from a year previous, and is one of an instance of the common vernal recurrence. The case is of particular interest in connection with the old views of the relations of pneumonia and malaria of which we do not hear very much now, but about which two generations ago the physicians of the South were so much perplexed.

These are the only two instances in a series of nearly three hundred cases

of malaria and three hundred and nine cases of typhoid fever, and with blood examinations in all, in which the malaria has occurred with another infection.

Dr. F. P. Kinnicutt: Dr. Thompson's observations are certainly most interesting. I am not familiar with any other exact observations showing the double infection with the malaria and typhoid bacillus. His first case certainly would seem to be a very distinct one of double infection. There can be no doubt in regard to the diagnosis of typhoid fever, and the plasmodium of malaria was found.

I think we should be guarded in our conclusions in regard to the frequency of these double infections until we have further observations. It is certainly very possible to mistake a remittent fever for typhoid; and in illustration of this, I present a chart of a case which was admitted to St. Luke's Hospital during the summer months a year ago. The patient was admitted with a diagnosis of typhoid fever. Before admission he had been ill for a week with apparently the usual symptoms of typhoid. He had enlargement of the spleen and a very few suspicious spots on the surface of the trunk. There were no abdominal symptoms beyond a little puffiness of the abdomen. It was regarded as an ordinary but severe case of typhoid fever, the temperature running constantly high—105° or thereabouts. The man passed into a semi-comatose condition, the tongue became dry, brown, and cracked, and the prostration was very great. At the end of the fifteenth day, on the twenty-third day of his illness, the temperature rather suddenly fell, after a tub bath, to normal; rose the next day one degree, then fell and rose a degree and a half, and then fell to normal, where it remained for five days, when it suddenly rose again, and in three days had reached 106°. The very sudden and great rise of temperature caused an examination of the blood to be made, and it was found to contain a large number of the organisms of malarial fever. Subsequently he was given rather large doses of quinine, and in two days his temperature fell not to rise again while in the hospital. He was discharged cured.

The interesting point in the history is this, that the man doubtless had a remittent fever throughout. Subsequently we ascertained that he had come from Central America to New York; that while in Central America he had some indefinite chills, had lost his appetite, etc. On arriving in New York, he went into a boarding-house, and from there came directly to the hospital.

If you will study this temperature chart you will see how closely the curve resembles that of typhoid fever. The practical lesson to be deduced is that the blood should be examined in every case of fever that comes into the hospital wards.

Dr. G. L. Peabody: It seems to me worth while to call attention to the fact that there are other chills occurring in typhoid fever than malarial chills, which are of more importance. Of course, by the examination of blood it is possible to differentiate between the chills of pyæmia and

those of malarial fever, but clinically they are practically identical, inasmuch as the malarial chills do not recur with any great regularity in typhoid when they do occur. It has happened to me twice to have severe chills late in typhoid fever which were pyæmic in character, as proved at autopsy by finding a number of small abscesses in the kidneys. It has also happened to me very often to have severe chills followed by elevation of temperature as a symptom in typhoid which did not affect the subsequent course of the disease, the patients getting well without the administration of quinine, and getting well apparently as other patients do who do not have these symptoms. In other words, it seems to me that we may have chills in typhoid fever apparently of malarial origin without their affecting the prognosis and without necessitating the administration of quinine.

I agree with what has been said, that it is very important for us not to put our seal of approbation upon the idea that typhoid fever with malaria is a frequent combination. That is a fallacy which prevails very largely in the country districts of New York. It is still common in many districts of New York to call every case of typhoid fever "typho-malarial" fever, and to poison every such patient with quinine.

Dr. Janeway: This question of chills in typhoid fever and their causation is a very interesting subject. We ought to recollect that when a chill comes in the course of typhoid fever, it is not necessary to suppose that it is due to the intercurrence of other disease. It is due in many cases to treatment. If we give the modern antipyretics in large doses, chills will occur, which are due simply to the fact that the temperature has been depressed, and then it rises and this rise is accompanied by mild and sometimes by severe chills. Drop your antipyretics and the chills disappear. This is true especially of the coal-tar products.

The fact of the combination of the two diseases is proven at times by the phenomena found at autopsy. The occurrence of typhoid lesions and of pigmentation, showing the coexistence of lesions of the two diseases, I have seen; and I have seen it in one case, which was of great interest, where the clinical history did not show malarial symptoms. The case was of great interest in another way. The woman was delivered before a class of medical students in the amphitheatre of a hospital, with forceps, and was taken with the initial symptom within thirty-six hours after such delivery. As the man who had delivered her was the demonstrator of anatomy, he of course supposed that the case was one of puerperal fever, and she was removed to the hospital where I had charge, and there at first we did suppose that the case was going to be one of puerperal fever. The discharges from the uterus, however, were perfectly normal and there were no phenomena pointing definitely to puerperal fever; simply the phenomena of typhoid. She died in the third week, and the lesions were those of typhoid fever with the addition of pigmented spleen, pigmented liver, and some pigmentation in the capillaries in other situations. To my recollection the clinical history did not show phenomena of malaria besides those of typhoid.

That we have malarial conditions coexisting with typhoid, clinical histories and the administration of quinine have proved to me beyond doubt; and we have to say sometimes, that we have malaria coexisting with typhoid fever. I do not believe in giving the name "typho-malarial fever" to this combination. I think we should call it typhoid fever with malarial coexistence. One reason for this is that physicians who give the name "typho-malarial" to it, assure the family that it is not typhoid fever, and thus take away the preventive measures for typhoid fever, and so do much harm. I have known cases where the use of such a term has been the cause of increased infection, for it has rendered the people satisfied, and the disease has spread in consequence.

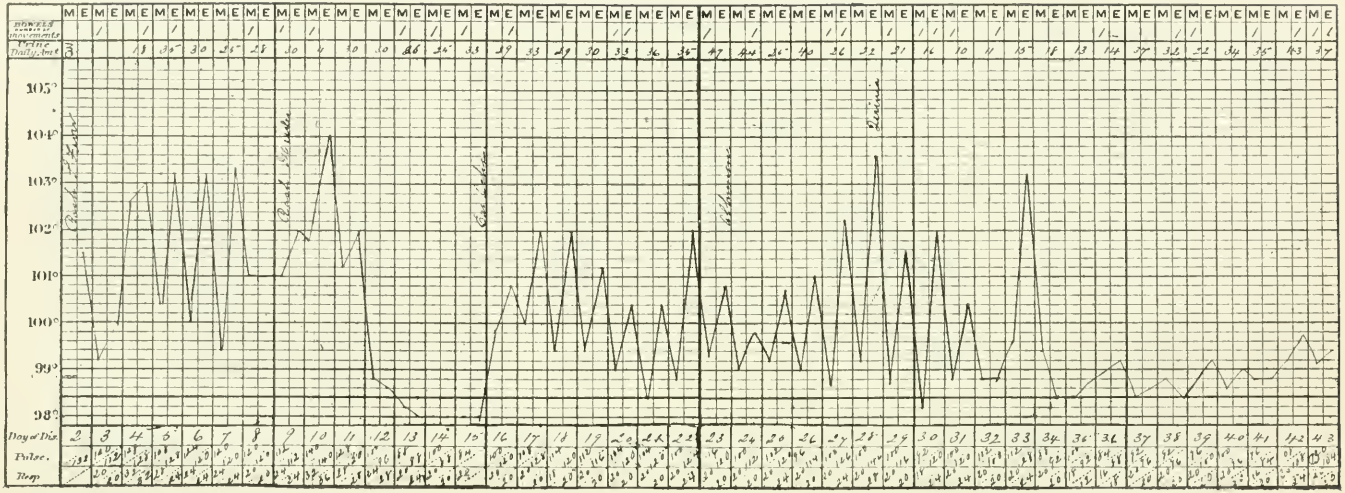
Dr. Geo. M. Sternberg: Dr. Thompson's first case shows very clearly a mixed infection, which I judge, in so pronounced a form, is rather a rare thing. The other cases show the development of malarial fever during convalescence from typhoid—an occurrence which I believe is not very rare in malarial countries. I have risen for the purpose of calling attention to the fact that the cases presented by Dr. Thompson differ from those commonly diagnosed as typho-malarial fever in the Southern States, and in other sections of the country. These cases usually are of a comparatively mild character and do not present distinct malarial paroxysms characterized by a chill and sudden rise of temperature. The temperature is often quite irregular during the first week, having a remittent character. This leads the doctor to make a diagnosis of malarial fever and to prescribe quinine. In the course of the second week, however, the difference between the morning and evening temperature is not so marked, and he gives up his quinine, saying that the fever has assumed a typhoid type. It has really been typhoid from the outset, although in these cases the symptoms are not so well defined as in typical cases of this disease. There is apt to be constipation rather than diarrhœa; rose spots are scanty or absent, and yet these cases often occur side by side with severe cases of typhoid fever, and I believe them to be mild cases of typhoid infection. I have studied the statistics of continued fever which occurred in our armies during the late war, when our army surgeons classified these fevers as simple continued, typhoid, and typho-malarial. These statistics show that the mortality from the fever diagnosed as typhoid was very much in excess of that from the form denominated typho-malarial fever. If the so-called typho-malarial fever was a mixed infection, it presented the anomaly of being less fatal than simple typhoid fever. In other words, if it was typhoid with a malarial complication, the complication modified the severity of the specific fever. This hardly seems probable, and, as already stated, these cases are, in my opinion, mild atypical cases of typhoid fever. It is possible, however, that we are mistaken in this, and that there is a widely prevalent endemic fever which is specifically distinct from typhoid. If so, it is equally distinct from the malarial fevers, as quinine has no effect in terminating its course; and, in any case, the name

typho-malarial seems to me to be a mistaken one, which can only lead to confusion of ideas.

Dr. J. C. Wilson: I hope this Association will not commit itself to the use of the term "typho-malarial." There can be no doubt that this term, so catching and apparently so proper at the time it was coined, has done an incalculable amount of harm—has stood in the way of the advancement of our knowledge of the fevers. This unfortunate term has delayed, for perhaps more than a generation, a clear knowledge of the fevers of the South. Even where typhoid fever has been generally recognized as a nosological entity altogether distinct from the malarious diseases, and especially in eastern Pennsylvania, New Jersey, and elsewhere in the middle and eastern sections of the country, the term is habitually used to designate obscure cases the symptoms of which have not corresponded to the descriptions of the text-books, and has acted as a serious obstacle to clear diagnosis.

Dr. Thompson's opportune presentation of these cases reopens the whole subject in a most fortunate way. His paper shows how much clearer, how much more definite the work of the medical profession is becoming with our newer and more exact methods of investigation. I believe, with Dr. Janeway, that we must recognize in future a form of disease, a modification of enteric fever distinctly due to the action of the malarial infecting principle, whether previously acquired by the individual or acquired during the course of his sickness. One of the charts shown by Dr. Thompson is apparently susceptible of the latter explanation. It is that of the case in which, at the end of convalescence, three malarial paroxysms occurred on successive days. Is it not possible that during the patient's illness with typhoid, by some mischance malarial infection had taken place, and that the condition of convalescence from enteric fever has rendered the individual curiously susceptible to the secondary infection, which is in nature and time quite independent of the enteric infection?

Dr. J. H. Musser: It is with some hesitation that I rise to report a case of mixed infection, or rather of repeated infection, because of the lack of an important link in the chain of evidence; yet I think the conclusions are fully justified. The case is that of a child nine years of age. In the spring of 1893, this child, together with another member of the family, had an attack of intermittent malarial fever. In the same year it had a second attack of malarial fever which yielded to anti-periodic treatment. In December of last year measles broke out in the family, and on the third day after the other children had measles, this child had scarlatina. Four days after the temperature became normal, measles developed in the child. This was followed by otitis, and then Dr. Grayson took charge of the ear inflammation. The chart indicates the time of occurrence of these complications and of the onset of Bright's disease. These infections took place during the desquamative stage of scarlet fever. During the course of the otitis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intermittent fever developed in distinctive paroxysms. Fearing that the intermittent fever was due to the affection of the ears, the use of quinia was withheld and the local infectious process carefully studied. Quinia was withheld for a considerable time on account of this indecision. The little fellow was so sick that I could not bear to have an examination of the blood made. The local inflammation subsided, and during its subsidence (care being taken to exclude mastoid disease and inflammation of the sinuses) I was compelled to give quinia, with immediate and prompt relief to the intermittent fever. In this case I feel that we undoubtedly had a malarial infection following rapidly upon an infection of scarlet fever, an infection of measles, and at the same time concurrent with a streptococcus infection.

Dr. H. M. Lyman: It has occasionally been my fortune to observe cases that have presented features like those exhibited by the chart of Dr. Thompson, in which typhoid fever ran its normal course and terminated apparently in convalescence, and then there were successive chills with rise of temperature following. The cases that Dr. Thompson has recited show clearly that malarial infection was the cause, but in the cases to which I refer there were certain differences. The patients had successive chills, occurring at somewhat irregular intervals, usually quotidian, but not at any certain hour of the day, and not yielding to quinine, being also accompanied by slight jaundice. These cases have been explained by French observers and others as due to the migration of the typhoid bacilli and other pathogenic germs, from the intestine into the biliary passages, producing angiocholitis, which is accompanied by chills that do not yield to quinine and is accompanied by a certain amount of jaundice running its course somewhat indefinitely, and being far more benefited by local measures addressed to the liver than by the administration of anti-periodics. These cases are occasionally seen and should be kept in mind in judging of these varied complications that accompany typhoid fever, especially during its convalescent period. These cases must be carefully differentiated from the pyæmic cases, some of which are notable and easily recognized before their conclusion.

Dr. F. C. Shattuck: It has seemed to me that some of the inexplicable chills which occur during convalescence from typhoid fever may be due to phlebitis in internal and inaccessible veins. The chills and subsequent pyrexia may be very similar to that accompanying phlebitis in superficial veins. As Dr. Kinnicutt remarks, the importance of a routine blood examination is apparent. A phlebitis would be accompanied by leucocytosis.

Dr. James E. Reeves: The subject before us is so important, and I have so much interest in it, that I am induced to add a few words to the already lengthy discussion.

In a paper on the "Natural History of Enteric or Typhoid Fever," which I had the honor to read before the Association in 1890, the same question was briefly noticed, and the point made that the clinical history of the so-called typho-malarial fever met with at all seasons in Chattanooga and the Southern country round about, is in every essential particular unlike enteric or typhoid fever with which I have been acquainted for more than forty years.

Until my removal from West Virginia to Chattanooga, in 1888, I had not seen this form of "continued malarial fever" which has here been denominated "typhoid fever complicated by malarial fever." While true enteric or typhoid fever may in some cases be so complicated by malarial intoxication as to render it extremely difficult, if not impossible, to distinguish the original or leading element of the clinical history, it cannot, I think, reasonably be assumed that all cases of enteric or typhoid fever in the Southern country are thus more or less complicated and masked by malarious influence; in other words, that we should not more frequently come across in the higher levels and most salubrious districts typical enteric or typhoid fever—uninfluenced by malarial complications—just as the disease is met with in nineteen cases out of twenty in Washington, Baltimore, Philadelphia, New York, Boston, and all other Northern and Eastern cities, towns, villages, and country districts.

The fact that such pure cases of enteric or typhoid fever are even more infrequent in Chattanooga and other Southern communities than the occurrence of mixed cases—such as the three cases upon which Dr. Thompson's able paper is founded—in New York City and elsewhere in the North and East, is to my mind a most forcible answer to the question at issue before us.

The doctrine of the blending of types is not a new proposition. In 1852, Prof. Samuel H. Dickson contributed a paper to Vol. V. of the *Transactions of the American Medical Association* in its support. This was followed in 1856 by a communication on the same subject to the *Buffalo Medical Journal*, from Prof. Austin Flint.

But while fully accepting the fact that these two very different morbific agencies may coexist within the organism and display simultaneously the symptomatic phenomena peculiar to each, neither of the distinguished authorities just named believed in the *conversion* or metamorphosis of one species into another. The poison of malaria is a distinct quantity producing certain well-known symptomatic phenomena, and culminating either in intermitting or remitting fever, and these forms only; while the contagium of enteric or typhoid fever gives rise to certain other morbid results peculiar to that disease, and none other. In other words, each disease proceeds from the introduction into the system of a specific poison; and when the two poisons gain entrance into the body at the same time, a commingling of symptoms truly confusing even to the expert clinician may be the result; but the conjoint action or association of the two specific poisons can never

give rise to a distinct or independent species. It is a natural law that hybrids are monstrosities and incapable of multiplication. The presence of malaria in conjoint action with the contagium of enteric or typhoid fever may, possibly, produce attenuation in some degree of the poison of the latter; but the union of the two elements cannot give origin to a distinct permanent type of fever.

Enteric or typhoid fever is communicable from person to person and cannot spring up *de novo*. In its prevalence, it may assume different degrees of severity, appear either in isolated cases with but feeble contagious power, or seize whole households, attack whole neighborhoods, or spread over large districts, according to the prevailing "epidemic constitution." Such, indeed, is not the history of the "continued malarial fever" we have in the South. The clinical features are also as markedly different. The temperature-curve is more variable and uncertain as to time of rise and fall; the gastro-hepatic involvement more pronounced, with nausea and vomiting, broad, flabby, creamy-colored tongue, bitter taste in the mouth, greenish tinge of the fluids ejected from the stomach, and the *absence*, as a rule, of diarrhœa, tympanitic distention of the abdomen, epistaxis, rose-colored spots, dulness of hearing, mental hebetude, or morbid vigilance and delirium—all these clinical traits afford, I think, good ground for the belief that the fever about which there is so much difference of opinion among the physicians of Chattanooga and elsewhere in the Southern States, is *not* enteric or typhoid fever; neither can it be called, without qualification, *bilious remittent fever*.

An attack of enteric or typhoid fever affords immunity, usually for the remainder of life. This I have observed to be as constant as the safety from a second attack of measles, scarlet fever, smallpox, or yellow fever. In all my experience, I have never known a person to have the disease a second time. After an attack of "continued malarial fever," the patient has no such immunity, but is all the more liable to a second attack. In fact, his liability increases with each successive attack; and it is no uncommon observation to find a person who has had the disease several times. In the treatment of these cases, in the beginning, quinine is not well borne, and is often more detrimental than remedial.

After convalescence from enteric or typhoid fever, there is in most cases rapid accumulation of flesh which is out of all proportion to the muscular strength; the hair falls out; and in due time the person is either greatly improved in general health or quickly succumbs to tubercular consumption, if he have such tendency. After convalescence from "continued malarial fever," the subject is for several months in poor health and strength, his countenance is sallow, he does not gain his accustomed flesh, his digestion remains feeble, and he is inclined to drop into "chills and fever."

The greatest number of enteric or typhoid fever cases occurs within the seven years between the ages of eighteen and twenty-five. On the other hand, "continued malarial fever" attacks more frequently children below the age of ten years than above that age.

How much, as suggested by Dr. Janeway, medical treatment may have to do in formulating the temperature-range in these so-called typho-malarial cases, is truly an unknown quantity; but it may be safely said it cannot deprive enteric or typhoid fever of its characteristic features.

For all these reasons, may it not be true that there is an unrecognized specific fever, intermediate in its march and complications between enteric or typhoid fever and the forms of malarial fever, *which should be called by some other name?* To this end, I have already made some observations.

Dr. George Dock: It is very much to be hoped that Dr. Thompson's observations will be repeated by others. That is the only way in which the relation of malarial infection to typhoid can ever be made clear. I do not see any danger of perpetuating the name "typho-malarial fever" by observations or discussions of this kind; on the contrary, this is the way to give the term its proper status. As far as these cases that have been reported are concerned, they go a very short way in showing the existence of double infection in any proper sense. In Dr. Thompson's first case, although the malarial infection occurred sooner than usual, it is difficult to see by the temperature chart that there was any malarial element in the symptomatology before the chills occurred, a thing which the variable latency of malaria explains. In Dr. Osler's first case, which is extremely important, the malarial infection seems to have had no influence at all on the course of typhoid. It is worth while to call attention to the fact that Dr. Kinyoun, of the Marine-Hospital Service, a few years ago (1890) reported patients who had typhoid fever and in whom he also found the malarial organisms. He also cultivated what he thought were typhoid bacilli out of the stools, a point on which he would not now, perhaps, lay much stress. From the clinical features of the cases, I think they were cases like the cases mentioned by Dr. Thompson, in which the malarial organisms were found late.

It was held by Woodward and often asserted in the South, and also in the North, that the so-called typho-malaria is a milder disease than typhoid alone. I do not see, from the charts that have been shown to-day, that this is likely to be so. It is only by carrying out such observations further, and examining very large numbers, that this can be demonstrated. While practising in Texas, I made especial efforts to find cases of double infection. I offered to go anywhere where a doctor had a case of continued malarial fever or typho-malarial fever, and I examined quite a number, with negative results. I made autopsies in six cases diagnosed as typho-malarial by experienced men, and in all cases they were nothing but typhoid fever. I became convinced, therefore, that fatal cases having the supposed malarial aspect were not uncommon.

I am glad the fact has been mentioned that physicians in the North have been guilty of using the term "typho-malaria." Three or four years ago, a very good editorial appeared in an Albany medical journal speaking of the fact that in New York State, in the interior, the diagnosis is often made.

In Michigan it is a very common occurrence. I have made an autopsy there, in one case, diagnosed as typho-malarial fever by one doctor, continued malarial fever by another, and remittent malarial fever by another. The autopsy was to decide the diagnosis. I found the patient died of intestinal perforations with no evidence of malaria In another case, diagnosed malarial remittent and typho-malaria, death was due to intestinal hemorrhage.

Only a few days ago a patient was admitted to my wards with what I diagnosed as an extremely severe case of typhoid in the third week. His doctor had said that he had not typhoid fever, and came to see me and tried to argue that it was a malarial fever, or at any rate not typhoid. The patient died from hemorrhages. Unfortunately I could not get an autopsy. There were no plasmodia in the blood and no sign at all of the double infection.

As I said in the beginning, such observation ought to be repeated in every case of typhoid, especially in those parts of the country where the term typho-malarial is used.

Dr. W. Gilman Thompson: The discussion has already exceeded in interest and length anything that I had anticipated. The object of my paper was to make a contribution to the natural history of the malarial organism, rather than to discuss the wide subject of chills in enteric fever. The three cases reported by Dr. Osler, taken in connection with mine, are of interest in proving that this organism may be present throughout the period of infection of typhoid fever. It may manifest its influence before the typhoid germ becomes active or during its activity, or its effect may not be exhibited until the typhoid fever has run its course. Just how far the malarial germ influences the action of the typhoid germ, is a question which is still undecided. In the first case presented, which is the one of chief value in regard to this subject, the presence of the malarial germs did seem to influence the disease considerably, and I have never seen, in cases of chills occurring from various causes in enteric fever, another that could be influenced with quinine to such an extent.

I think we may deduce two practical points from this discussion: The first is the value of routine examination of the blood for malarial organisms in cases of enteric fever that are at all irregular. Secondly, we should determine the value of giving quinine in those cases where malarial organisms are present.

EXPERIMENTS IN ARTIFICIAL MELANOSIS.

By GEORGE DOCK, M.D.,
OF ANN ARBOR, MICHIGAN.

THE experiments here reported were made in the hope of throwing additional light on the disposal of malarial pigment, and, although the results have been disappointing, they seem worthy of brief record.

After the early observations on the inclusion of foreign particles by leucocytes had been made by Schultze (*Archiv für mik. Anat.*, Bd. i. p. 1), Cohnheim (*Virchow's Archiv*, Bd. xl. p. 1), and Hoffmann and Von Recklinghausen (*Centralblatt für die med. Wissenschaften*, 1867, No. 31), observations carried out with greater detail by Ponfick (*Virchow's Archiv*, Bd. xlviii. p. 1) and Hoffmann and Langerhans (*Ibid.*, p. 303), little interest was taken in the subject until a recent period, when Metchnikoff put forward the doctrine of phagocytosis, which depends on the properties of certain cells which had been made known by the observations mentioned.

Very early in the study of malaria the occurrence of cells containing pigment particles was noted. Some of these cells we now know were malarial parasites, but others were leucocytes or other body-cells with pigment derived from malarial organisms. Metchnikoff, early in his work on the subject (*Centralblatt für Bakteriologie und Parasitenkunde*, Bd. ii. p. 624) recognized the occurrence of phagocytism in malaria, and this has been observed and described by nearly all who have worked within recent years in the parasitology of malaria.

In ordinary cases of malarial fever pigment is found in polynuclear cells with neutrophile or amphophile granulations, the cells which on the warm stage show phagocytic action. In severe cases, especially in fatal cases, cells of a different kind, and containing pigment, are found in the blood and in certain internal organs.

These are much larger than the polynuclear leucocytes, have simple but often irregular nuclei, and on account of their size and properties are called macrophages. The origin of these cells is obscure. Metchnikoff believes they are of endothelial origin, and gives strength to his view by citing the phagocytic action of endothelial cells *in situ* in certain bacterial diseases.

In a case of pernicious malarial fever with large numbers of macrophages, however, I could find no evidence of inclusion on the part of the endothelial cells (*American Journal of the Medical Sciences*, April, 1894), and this contradictory result was one of the things which led to the present experiments.

My experiments were made in the pharmacological laboratory of the University of Michigan, and I take pleasure in expressing my thanks to my friend and colleague, Dr. A. C. Cushny, Professor of Pharmacology, for his valuable assistance in making the injections and in other ways furthering the experiments.

The method was as follows (from the results it does not seem necessary to give the details noted at the time):

The animals were chloroformed, one of the superficial veins of the hind leg exposed, and a canula tied in. The canula was filled with normal salt solution, and then from one to two cubic centimetres of physiological salt solution, rubbed up with lampblack to the consistence of blood, was slowly injected into the vessel, care being taken to avoid the entrance of air. The fact that the suspension passed into the circulation was readily observed. The vessel was then ligated and the incision closed.

As soon as the injection was made the blood was examined by puncture of the ear, and these examinations were repeated at frequent intervals. In addition to the fresh drop, examined without any addition, cover-glass preparations were made and examined. The injections were made once a day. The largest number made in one animal was eight. One dog died just at the end of the first injection, probably from too rapid introduction of the fluid. Another died after the second injection, apparently from anæsthesia. The longest time allowed to elapse after the injections was two weeks. In the other cases the animals were killed at intervals of one day to one week after the last injection. In all six dogs and one rabbit were used.

The leucocytes of the dog were examined with reference to their characteristics before the injections were begun, with the following results:

75 to 90 per cent. (in different animals and at different times) are polynuclear cells. These have nuclei resembling those of man, but the protoplasm does not stain so deeply with neutral dyes (Biondi's solution). A few of them have fine granulations which take a faint tint with eosine.

6 to 15 per cent. are large mononuclear and transition cells requiring no special description.

3 to 5 per cent. are large lymphocytes.

1 to 3 per cent. are polynuclear cells with eosinophile granules, but the latter are much less numerous than those in corresponding cells in man.

It was not part of my object to estimate the total number of leucocytes, but the cover-glass preparations show some interesting things, sometimes evident in the fresh drop. The proportion of leucocytes was found to vary greatly, and the variations could not be ascribed to feeding, or to the tying-down, anæsthesia, etc. In one case, for example, the dog showed a remarkable number of leucocytes about three hours after he had swallowed a large meal, and it was supposed this was a digestion leucocytosis. Soon after, however, just after chloroforming, he vomited up the whole meal entirely undigested.

The results of the injections are as follows:

The lampblack grains appear in the blood of the ear within a few minutes, but do not appear in the leucocytes earlier than fifteen minutes—often only as late as thirty minutes. The grains then continue to circulate for from four to twenty-four hours.

The only leucocytes in the peripheral blood which contain pigment are the polynuclear cells.

The organs were examined by fixing warm pieces in sublimate solution, hardening in alcohol, cutting in paraffin, and staining on cover-glasses to which the sections were fastened by heat after floating out in warm water.

In the organs the relations of the pigment vary according to the time the animal lived after the injection. Even in animals killed early, or in the one dying after the first injection, the pigment is not

evenly distributed in the body. Most of it is in the lungs, next in the spleen, and then in the liver, so that all these organs show a grayish discoloration, even after one injection. The other organs contain very small quantities. The bone-marrow contains more than the remaining tissues. The brain and cord contain little or none.

The veins just above the ligatures show a good deal of pigmentation in the endothelium as well as in the other coats, much of it being evidently in the lymph spaces.

In the frequent thrombosed vessels in the lungs there is often proliferation of the endothelium. In these parts pigment occurs in oval or spindle-shaped cells, with round or oval nuclei, and also in cells having the characteristics of polynuclear leucocytes in and around the vessel walls.

In the walls of unaltered vessels pigment can be seen apparently in endothelial cells, and in smear preparations from the lungs cells containing pigment occur which seem to be endothelial cells. These are about the size of polynuclear cells, or sometimes twice as large, with a single round nucleus, and often have small vacuoles in the protoplasm.

In the spleen a large part of the pigment is free, even after the lapse of two weeks. The blood-corpuscle and blood-pigment containing cells of the spleen contain the lampblack grains frequently, and sometimes in very large quantity.

The spleen shows a great difference from that of malaria in that the macrophages are absent, since the blood corpuscle-holding cells have not, I think, been held to be identical with the former. It cannot be distinctly seen that the endothelial cells of the spleen contain pigment, nor does it occur in the dense connective tissue even after two weeks. The lymphoid cells of the spleen never contain pigment, although granules can often be seen in capillaries in the lymphoid areas, both free and in polynuclear leucocytes.

In the liver, in the early periods the pigment is largely in the portal areas, free or to a slight extent in polynuclear cells. Later, the granules approach the central veins, surrounding them and forming stellate injections of the adjacent capillaries. The granules are to be seen to a slight extent in the endothelial cells and in the cells of Kupffer, never in the liver cells or the epithelium of the biliary canals.

In two cases in the liver (four and eight injections) I found small collections of polynuclear leucocytes and pigment in dilated capillaries, without evidence of irritation around them.

The kidneys show a few fine grains in the glomeruli, and less frequently in the intertubular capillaries.

Neither here nor in any of the remaining organs are there deposits in endothelial cells.

From these observations the importance of the polynuclear leucocytes in the removal of foreign material from the blood is confirmed. The further disposal of the pigment I did not endeavor to work out. It appears, too, that the endothelial cells act in the removal of the pigment. Some of the older observers doubted this, and it must be said that it is often impossible to be sure of the position of pigment grains with reference to the endothelium. But from the method used in these experiments in the preparation of the sections it was possible to get very thin ones without distortion and to examine them with high powers (one-twelfth inch immersion lens), so that the danger of misinterpretation is much less than with the older methods.

Whether the absence of macrophages is due to a peculiarity of the animals used I do not feel able to say, but incline to the belief that in the diseases in which these are found (especially malaria, typhoid fever, pyæmia) there is a process at work other than the mere removal of foreign matter.

The peculiar localization of the pigment in the liver and spleen is of interest in connection with the part these organs play in malaria, and the inference seems legitimate that the other localizations which often occur, as in the brain, bone-marrow, and, as in the case of my own referred to, in the abdominal fat, are due to the effects of the malarial poison in the chemical sense.

ON LEAD PALSY IN CHILDREN; WITH A REPORT OF THREE CASES.

By WHARTON SINKLER, M.D.,
OF PHILADELPHIA.

A CAREFUL search through current literature and the text-books shows great paucity of material in regard to plumbism in young children. In an admirable and thorough article on lead-poisoning, by James J. Putnam,[1] this author remarks that the justification for his article "is found not in the abundance but in the meagreness of the present accumulation of facts relating to children, and the importance of taking steps toward increasing it." I have been able to find no other cases besides those which Dr. Putnam has quoted in the complete table which he has added to his paper.

Wilson, in *Pepper's System of Medicine*,[2] says: "Lead-poisoning is an affection of adult life. Of 102 cases, two only occurred in individuals below twenty years of age."

D. D. Stewart, of Philadelphia, whose article on poisoning by buns colored with chrome yellow attracted so much attention a few years ago, writes me that he made a thorough search through the literature of lead-poisoning when investigating these cases, and made notes of all nervous cases, especially those with brain symptoms. He found many cases of cerebral disorders, like convulsions, which occurred in children, but none of paralysis. He also remarks that in German literature there are a number of accounts of whole families being poisoned by lead, through working and living in the potteries; but there are no records of palsies in children among these cases, though paralysis in the adults are common; and it was related that the children had headache and convulsions.

[1] Encyclopædia of the Diseases of Children, vol. iv. p. 615.
[2] "Chronic Lead-poisoning," System of Medicine, vol. v. p. 686.

Among Stewart's cases of chronic lead-poisoning from eating the chrome-yellow buns, seventy-nine in number, there were many children. These were specially affected with convulsions, but there were no cases of wrist-drop or other palsies among them.

There is apparently no reason why children should not be as susceptible to lead-poisoning as adults. Children are as much exposed to the dangers of lead-poisoning, except in those cases which occur among workers in lead—as, for instance, painters, manufacturers of white lead, and those employed in potteries.

There are many cases on record in which children of various ages have been seriously poisoned by the absorption of lead into the system. On the other hand, in epidemics of lead-poisoning from drinking-water, the proportion of cases of children is small. In the epidemic which occured at Tredegar, England, reported by Dr. Brown, and quoted by Putnam, there were no serious symptoms in any person under eighteen years of age, out of fifty-two cases of well-marked lead-poisoning.

Putnam refers to another epidemic, in which thirty-eight persons were exposed to poisoning through drinking-water. Thirteen were affected; but no children were attacked, although there were eight among those who had been drinking the infected water. It is probable, therefore, that children are not so liable to lead-poisoning as adults; and this is no doubt due to the fact of their possessing more active powers of elimination; their greater bodily activity and the greater activity of all of their secretions eliminating the lead from the system quite readily.

The sources of lead-poisoning are so numerous that it is remarkable that more cases of infection do not occur. Drinking-water in cities, from passing through lead pipes, frequently becomes charged with lead. Lead is to be found in cooking utensils, in red rubber which is sometimes used for making nipples for nursing-bottles, in the solder used in cans, coverings of sweetmeats, and in chromate of lead which is used in coloring toys, cloths, and other articles.

It is evident from the cases which have been recorded, in which a large number of persons have been equally exposed to the danger of lead-poisoning, that the degree of susceptibility varies, as but a small proportion of the persons exposed are attacked.

The symptoms of lead-poisoning in children which have been most

frequently noted are disturbances of digestion, such as colic and vomiting; and the cerebral symptoms indicated by headache, convulsions, and stupor. Chronic lead-poisoning is most likely to be manifested by a general loss of flesh, failure of appetite, and the earthen hue of the skin, with a jaundiced condition of the conjunctiva. In chronic lead-poisoning disorders of digestion are most common; constipation, attacks of colic and vomiting frequently occur, and there are other evidences of disease of the stomach in the defective assimilation which exists. In other cases symptoms of kidney disease are shown; and it is well known that there is a form of nephritis due to accumulation of lead in the kidneys.

The symptoms dependent upon disease of the nervous system due to lead-poisoning are motor and sensory. The most common of these, of course, is paralysis of the extensor muscles of the forearms. In children, however, it is a noteworthy fact that the paralysis is as liable to affect the lower extremities as the upper. There are but few cases reported in which sensory disturbances have been met with in children. Cerebral symptoms are not uncommon in children. The lead encephalopathies in children have been frequently met with, especially, as already remarked, among the cases reported by Stewart, and Putnam refers to other cases.

The cases of lead palsy in children which are quoted by Putnam are, first, that of a girl of eight years, reported in the *Lancet*, who suffered from paralysis of all four extremities, from the use of Sheffield drinking-water; and a similar case which was related by Seligmüller, who credits it to Duchesne.

H. D. Chapin[1] gives a history of two cases of lead palsy in children. ' I will detail these at some length because of their curious similarity to the cases which I shall report later.

The father was a painter, and kept paint in the house, so that the children were constantly exposed to the influence of it. They enjoyed good health until December 25, 1882, when the room in which the children lived was painted. On January 1, 1883, one week later, F. W., aged seven years, was seized with cramps in the stomach; on the next day R. W., aged five, complained of the same symptoms. The pain lasted for four weeks, and there was intense thirst. There

[1] New York Medical Record, 1884, p. 546.

was then pain and soreness in the legs, and the children were averse to walking. By the last of January they could not stand. They then improved somewhat, but during February another similar attack occurred. There was pain, followed by paralysis, and the loss of power lasted much longer than the first attack. On May 3d, a third attack occurred in one boy, in which the hand was affected. The children now came under Dr. Chapin's care. They could walk with difficulty, and a blue line was observed upon the gums. They were lost sight of for a year, when they were examined again by Dr. Chapin. They were worse than they had been before; they were utterly unable to walk, and pains throughout the body were complained of. The teeth were loose, the gums were spongy, and there was headache. The muscles did not respond to faradism or galvanism, but sensation was normal. The house in which they lived had been cleared of paint a year previous, and there was nothing to account for the repeated attacks.

The children were admitted to the hospital, and after treatment they improved greatly and were able to walk somewhat. An examination of the urine showed the presence of lead. There was partial paralysis of the anterior leg muscles, and these showed the reaction of degeneration.

Dr. Chapin called attention to the striking resemblance of these cases to spinal paralysis of infancy. This writer also related the case of a child two and a half years of age, in which applications of a solution of acetate of lead were applied to a splinter wound. In four days both legs were paralyzed, but the child soon got quite well. This is, I think, rather a doubtful case of lead paralysis.

The sixth case is reported by Putnam, from the records of the Children's Hospital, Boston, in which a girl of six years, after having been exposed to a freshly painted house, had attacks of vomiting, which affected her at intervals for two weeks, followed by weakness of the legs, toe-drop, and waddling gait. A month later there was weakness of the fingers and the wrist; the extensor muscles were affected in both arms and legs, and the knee-jerks were absent. Two months later the paralysis had disappeared, but the legs were easily fatigued.

A seventh case was reported by Miller,[1] in which a child of four

[1] New Orleans Medical and Surgical Journal, 1873, vol. i. p. 198.

years was poisoned by the drinking-water; but the writer merely observes that there was a paralytic state.

A case is reported by Letheby of a child of six years who took acetate of lead in doses of one-fifteenth of a grain two or three times a day for nine weeks. There was loss of flesh, colic, paralysis of the limbs, convulsions and coma, followed by death, which occurred two days after ceasing to take the medicine.

These constitute all the cases of lead palsy in children which I have been able to find, except a case reported by Suckling,[1] of a boy of fourteen years, who worked in zinc and lead for eighteen months, and who had evidences of multiple neuritis, without other symptoms of lead-poisoning.

The three following cases came under my observation at the Philadelphia Orthopædic Hospital and Infirmary for Nervous Diseases. The parents were healthy and had nine children. One child died of spinal meningitis at five years of age. It had, from birth, a large head. Another child died of convulsions at three years of age. Four other children are perfectly healthy, and the remaining three are the cases of which I will relate the histories.

The father is a house painter by occupation, and had his shop in the house in which he lived. The children frequently played about the room in which he kept his paints, and often got the paint on their hands and faces, and sometimes were seen to put it in their mouths.

Case I.—Sarah McD., aged ten years and six months.

Previous history. Her health had always been good previous to the onset of the present trouble. She cut her teeth and walked at an early age, and never had any intestinal disorders.

She was brought for treatment to the Philadelphia Orthopædic Hospital and Infirmary for Nervous Diseases, in July, 1889. About one month previous, that is in June, 1889, she awoke in the morning with partial loss of power in the legs. She had fever of short duration, and there was constipation and some vomiting, but there was no colic. The weakness of the legs steadily increased, and pain in the legs was complained of. Four weeks later the arms became weak, and there was gradual wasting of all the limbs. The weakness and atrophy were most marked on the right side.

The child was treated as an out-patient, by means of electricity, and in October, 1889, she had almost completely recovered the use of her legs.

About one year later, that is in June, 1880, she grew gradually weak for

[1] British Medical Journal, 1888, vol. i. p. 649.

about a week. She then lost the power of standing, and could not use her arms. In this attack there was fever, vomiting, and constipation, but no colic. There were no convulsions, no coma, and no headache.

On July 14, 1890, she was admitted to the hospital. Her condition was then as follows:

There was loss of power in all of the muscles of the legs, more or less complete; and there was complete wrist- and ankle-drop. The patient was unable to use the hands or arms, except that she could slightly move the arms at the shoulders. There was great muscular wasting, but no changes in sensibility. The patient's mind was clear, and her general health was good.

The electrical examination showed absence of response to the faradic current in the extensors of the legs, thighs, and forearms, and diminished reaction in the flexors to galvanism.

The reactions to the galvanic current were as follows:

Right tibialis ant. and common extensors . .	R D
Right peronei	K cl > A cl.
Left tibialis anticus and common extensors .	K cl = A cl.
Left peronei	K cl > A cl.
Left forearm extensors	R D
Right forearm extensors	K cl > A cl.

The patient was treated with daily faradization and massage, and in about four months she was able to walk about and to use the arms freely. She was discharged greatly improved, November 8, 1890.

She was examined on May 17, 1894, and her condition was as follows:

Both feet are flat, and foot-drop is marked on both sides, when sitting. The left great toe is abducted, and all of the toes of the right foot are abducted, the great toe especially. This toe is also rotated to an angle of about 90°, so that its dorsal surface points laterally. The patient is unable to flex the feet. The left leg is a little smaller than the right. There is no wasting in the arms, and the muscular power in both is good. In walking, there is a tendency to walk on the toes, on account of a slight contraction of the tendo Achillis. The patient's general health is good, and the gums are free from discoloration or disease.

The eyes were examined by Dr. A. G. Thomson, who made the following report:

Pupils are equal, and react normally to light; disks a trifle red; outlines of disks well marked; no lesions of fundus; muscular balance good; form and color fields normal. V.=20/20 both eyes.

Case II.—Harry McD., a brother of the preceding patient, was admitted to the hospital July 11, 1892. He was six years of age; was born normally, and was breast-fed. He began to cut teeth at the age of three months. He was healthy until the sixth month, when he had convulsions, which lasted three days. The spasms were general, but there was no subsequent paralysis. When sixteen months old, he had entero-colitis. He began to walk at

fifteen months of age. This child also had access to the room in which his father's paints were kept, and was frequently smeared with the paint. In November, 1891, he had an attack of fever accompanied by vomiting, loss of appetite, colic, and constipation. This attack lasted for about three weeks, when it was noticed that the legs and arms were weak. The arms could not be raised above the head, and the hands dropped at the wrists. There was loss of power in the legs, so that the child was unable to walk. Complaint of pain in the knees was frequently made. The legs and arms grew steadily thin, and the muscular weakness increased.

On admission the child was pallid and thin. He possessed normal intelligence; his digestion, appetite, and bowels were in good condition. The child was unable to stand, or to walk, and there is but little power in the muscles of the legs. The feet are in a position of ankle-drop, and attempts to flex the feet are futile. The arms can be moved slightly at the shoulders, but the power in the muscles of the arms and forearms is almost absent. There is complete wrist-drop. There is no facial paralysis.

Atrophy. There is marked wasting in the muscles of both arms and legs. There is no response to the faradic current; and there is great quantitative change in the extensors of the thighs, arms and forearms, to galvanism. R D. is present in the extensors of the left leg, and in the extensors of the right leg. The knee-jerks are absent, and the arm-jerks are decreased.

The patient was treated by massage and electricity, and steady improvement took place; so that in five months the patient was able to walk about unassisted, but the toes were dragged and the feet flapped in walking. The patient had gained flesh, and the color was good.

March 27, 1894. Condition of the boy was as follows: He walks with the feet far apart and the toes inverted. The left leg is much weaker than the right. The circumference of the right thigh is eight inches, the left thigh eight and a quarter inches. The right calf is six and a quarter inches, and the left seven inches. The knee-jerk is absent on both sides, and there is no reinforcement. There is left foot-drop, and the muscles of this leg are markedly wasted. The left hand is weak, and there is atrophy of the thenar and hypothenar muscles. The elbow-jerks can be elicited.

The electrical examination shows good response in the peroneal and calf muscles. The flexors of the thighs respond readily. R D is found in the tibialis anticus and extensor communis of both legs. The eyes show nothing abnormal.

Case III.—Eddie McD., aged three years, brother of the two previous patients, was admitted to the hospital July 11, 1892. He has always been healthy up to the present trouble. He began to walk at about the age of two years, but only with assistance. It was then noticed for the first time that the right leg was weak and that the foot was dragged in walking. He complained of some pain in the right knee at the same time. The leg continued to grow smaller until his admission to the hospital.

On admission, it was found that both legs were weak and that there was

complete wrist-drop. The extensors of the hand seem to be the only muscles which were affected, as the arms could be moved in all directions. The electrical examination showed reaction of degeneration in the muscles of both legs. The knee-jerks were absent on both sides. This patient also improved under the use of massage and electricity, and in five months he began to walk unassisted, but dragged the toes on both sides, more especially on the right side. The knee-jerks had returned and were slightly exaggerated.

March 27, 1894. The patient looks strong and ruddy. He runs about with freedom, but drags the right foot, and, on lying down, there is right foot-drop. The leg is wasted and there is inability to flex the foot. The thighs are each ten inches in circumference; the right calf is seven inches, and the left seven and a half inches. Sensation is perfect, and there are no trophic changes. The left hand is somewhat weaker than the right. The right knee-jerk is grossly exaggerated, but there is no ankle clonus. The knee-jerks on the left are slightly exaggerated. The electrical examination shows normal reactions in all of the muscles of the left leg and in the right calf. In the extensors of the right foot there is loss to the faradic current, and there is reaction of degeneration with the galvanic current.

In neither of these children was there any blue line on the gum observed, nor any diseased condition of the teeth or gums. The digestive organs were in fairly good condition when they were admitted to the hospital, and although they were thin and pallid, there was no distinct saturnine cachexia noticeable.

When the two boys were first admitted to the hospital, an attempt was made to examine the urine for lead, but this was not accomplished. They were readmitted in March, 1894, and after the iodide of potassium had been administered for several days, the urine was collected, evaporated, and carefully tested for lead on three different occasions: but no trace of lead could be discovered. The investigation was made in a careful and thorough manner by Dr. J. E. Talley, the resident physician.

The significance of lead in small quantities in the urine is not great, when we consider the statement of Putnam, in the article referred to above, in which he says that Drs. Comey and Worcester had analyzed for him the urine of more than 150 persons (who lived mainly in the neighborhood of Boston) not presenting symptoms of lead-poisoning, and found traces of lead in about 25 per cent. of them. Dr. J. Dickson Mann[1] gives as the result of careful study of two cases these conclusions: "That lead is slowly and more or less con-

[1] Brit. Med. Journ., Feb. 25, 1893.

tinuously eliminated by the bowels, and, *to a very much less extent*, by the kidneys; that when once deposited in the tissues it exists as a stable compound, over which drugs have little, if any power." He also asserts that iodide of potassium has absolutely no power as an eliminator of lead, although he admits that it may be beneficial in some other way in cases of chronic lead-poisoning.

In the cases which I have related, the symptoms presented were those of poliomyelitis; indeed, when Sarah McD., the eldest child, first presented herself at the Infirmary, I believed it was a case of that disease; and when she returned a year later with a relapse, I regarded it as a remarkable instance of a second attack of infantile spinal paralysis. It was not until the second child was brought to me for treatment that I suspected some common cause for the disease, and thought that it might be one of those instances of epidemic poliomyelitis due to microbic infection.

On inquiring into the history of the children, I found that their father was a painter, but the mother strenuously denied that they had been exposed to contact with the paints. When the third case was brought to me I asked my friend, Dr. J. H. Rhein, to visit the home of the children; and he discovered the fact that there was a great deal of white lead lying about, and that the children had frequently played in the paint room, and were often daubed with the paints.

The resemblance of lead palsy in children to poliomyelitis has been observed by several writers; and it seems possible that some of the cases which have been recorded as poliomyelitis may have been due to chronic lead-poisoning.

The pathology of lead-poisoning in children is generally considered as consisting in changes in the peripheral nerves; and these alterations are very closely allied to those met with in the ordinary forms of multiple neuritis. There is good reason to believe, however, that in many cases of typical lead-paralysis the symptoms are due primarily to the direct action of the lead upon the muscles. It is also probable, and this is also suggested by Putnam, that chronic lead-poisoning may produce typical changes in the anterior horns of the spinal cord, and thus give rise to a poliomyelitis, which is identical in its symptoms with the acute, or, so to speak, idiopathic form of the disease.

DISCUSSION.

Dr. J. J. Putnam: I have been much interested in Dr. Sinkler's cases, more so because they seem to confirm very strikingly the interesting observation suggested by the cases which I collected, that in children the legs are affected quite as early as the arms, and sometimes possibly earlier. Perhaps, in fact, it is more curious, that in adults the legs are not affected as early as the arms; in short, that we do not find the generalized type of neuritis in adults nearly as often as we do in children (although we do see this type oftener than is usually realized). I have also seen one or two adult cases where an exaggerated knee-jerk was present. This symptom is nowadays to be taken rather as the sign of an irritative condition of the nerves than as indicating an absence of such condition.

One thing that should be referred to in this connection is the experimental researches of Dr. Stieglitz, of New York, on lead paralysis in dogs, produced by giving small quantities of lead for some time. He found distinct focal changes in different parts of the spinal cord, and as much in the lumbar region as in the cervical region. It is some time since I have read the paper, but I think I am correct in saying this. He calls particular attention to the fact that the greater development of the disease in relation to the upper extremities in adults is probably due to the greater use which is made of the upper extremities by the adult, and he suggested that if we could find cases of lead paralysis in children, we very likely should find the other type of paralysis prevalent. The cases that I collected and Dr. Sinkler's seem to be decidedly confirmatory of this view.

Dr. Sinkler suggested that the infrequency of paralysis in children is due to the more rapid elimination of lead by way of the kidneys and intestines. Of course that may be the cause to some extent, but I cannot help thinking that there is something further behind. It seems to me that multiple neuritis in every form is less common in children. I have not, however, investigated this point and have not a positive opinion with regard to it.

Dr. A. Jacobi: Two cases of lead paralysis in children which I remember distinctly, were cases in which the arms and legs and feet were equally affected. One was a case of a boy who had been in the habit of eating the paint from his father's fence, and another one was a baby that had unfortunately been treated for very extensive eczema of the face and head with lead ointment. I do not suggest that in the latter case the child's skin absorbed the lead, for I saw the child picking his cheek and then putting his fingers in his mouth. Both of these were such cases—in which the feet were affected just as much as the hands.

Dr. M. Allen Starr: I would like to put on record two cases of lead palsy in children. They were very interesting cases which I was allowed to

watch in St. Mary's Hospital directly under the care of Dr. George M. Swift. They were sister and brother, the children of a painter, and, as in Dr. Sinkler's and in Dr. Putnam's cases, the paralysis began in the feet and later extended to the hands, the reverse of the ordinary adult lead paralysis. They presented very much the same general symptoms as those of Dr. Sinkler's cases, but a point that I wish to speak of particularly is that they were of very long duration, and one of the children, the little girl, died. I obtained an autopsy, and the spinal cord, although I subjected it to a very careful examination, I found perfectly normal. The peripheral nerves were all affected in the distal portion of the extremities. The main trunks of the nerves, the sciatic and the brachial plexus, were apparently normal. The degenerative changes in the peripheral nerves were very well marked. The cases are of interest as one was followed by autopsy.

APOPLEXY IN ITS RELATION TO THE TEMPERATURE OF THE BODY.

With a Consideration of the Question of Heat-Centres.

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The subject to which I wish to draw your attention to-day is that of the relation of apoplexy to the bodily temperature. By the term apoplexy I include both intra-cranial hemorrhages and softenings due to embolism or thrombosis. For several years I have been paying special attention to the effects of these insults to the brain upon the elevations of the temperature of the body, and I have accumulated sufficient material to justify me, I hope, in presenting some conclusions regarding the matter. The data which I have used in the present paper consist of observations upon over eighty cases of apoplexy in which an autopsy was made, and the nature and seat of the lesion noted. The points which I have sought to clear up in a study of these records have been: First, the general bodily temperature directly after an apoplectic stroke, and the later course of this temperature, if such is found to exist. Second, the temperature of the two sides of the body as compared with each other, and with that in the rectum. Third, the relation of the temperature change to the nature of the lesion, and, fourth, its relation to the seat of the lesion, including in this last a brief discussion of the subject of thermic centres in the brain.

As to the question of the direct effect of intra-cranial hemorrhages upon the general bodily temperature, my statistics (45 cases) show that in fatal cases, at least, there is on the first day after the stroke, a rise of rectal temperature, ranging from 100° to 102°,

averaging in my cases nearly, if not quite, 101.7°.[1] On the second day, if the cases are not immediately fatal, the temperature falls a little, and averages about 101° or 101½°. In acute softening, however (38 cases), there is rarely any disturbance of temperature, even in fatal cases, on the first day. On the second there is often a slight rise, so that the average is 99½° to 100°. Thus the presence of any temperature on the first and second days indicates a hemorrhage, and is, in addition, of serious import. Neither hemorrhages nor softenings produce a high temperature themselves. The fever, if it exists, is only 101° to 102½°, or, perhaps, 103°. In those cases in which there is a terminal high rise of 105°, or even 107°, a pneumonia, and sometimes even a gangrenous pneumonia, is found. I note only one exception to this in my cases, and then the clot was in the thalamus.

This general law, that the temperature rises after a serious hemorrhagic laceration of the brain, and does not rise after a serious embolic or thrombotic softening of the brain, has only few exceptions, as when the embolic process is extremely large, involving, perhaps, an entire lobe, or when it is seated in the pons or medulla, or when it is due to a septic focus; but such cases are so rare that they do not invalidate the general clinical rule which I have laid down. While I have based it mainly upon temperature observations of my own, because these have been taken with special care and a special reference to this point, yet they tally also with the records of others, so far as my investigation goes.

[1] Temperatures in cerebral hemorrhage:

Case A, 99¼° to 105¾°. Clot in corpus striatum and left ventricle.
Case B, 102°. Corpus striatum and right ventricle.
Case C, 101°. Surface clot.
Case D, 98°. Clot, corpus striatum.
Case E, 99°, 101°, and 103¾°. Clot, corpus striatum and optic thalamus.
Case F, 101½°, 101°, and 104°. Right corpus striatum and ventricle.
Case G, 101¼° to 105°. Surface.
Case H, 101½°, 100° to 103°. Right ventricle.
Case I, 100½°. Surface clot.
Case J, 99½°. Clot, optic thalamus, corpus striatum and right ventricle.
Case K, 101¼°. Surface clot.
Case L, 102½°. Clot, corpus striatum.
Case M, 100⅕° to 102¾°. Clot in ventricle.
Case N, 105.7°. Clot, optic thalamus and temporal lobe; delirium tremens.
Case O, 102°, 101°. Clot, frontal lobe (pneumonia).
Case P, 100.5°, 105°, and 105½°. Clot, optic thalamus.

These temperatures are all on the first to fourth days, except Case P, which runs to ninth day. Average temperatures of first day, 101°. All fatal cases.

The question of the *unilateral disturbances of temperature* after an apoplectic stroke is one that has interested me particularly, because it has seemed to furnish a more definite criterion of the nature of the injury. I have observed now seven cases of acute cerebral softening and three of cerebral hemorrhage in which the temperatures were taken in each axilla for some time after the stroke, and in some cases also in the rectum. Autopsies have been made also upon each of these cases. I have collected several other cases in which similar records have been made. I have also notes of a considerable number of cases in which the diagnosis of hemorrhage or softening could be made with approximate certainty. From the facts which I have thus obtained it has seemed to me that one can say with much certainty that in massive intra-cranial hemorrhages the temperature upon the paralyzed side is always somewhat higher than it is upon the sound side. In all my cases of cerebral hemorrhage there was on the first days, and continuously afterward, a greater rise of temperature on the paralyzed side, the average difference being one degree. On the other hand, in all my cases of acute softening, whether due to embolism or thrombus, there was practically no difference whatever between the temperature of the paralyzed and of the sound side.

These conclusions seem to me to be in accordance with what we might naturally expect. The sudden tearing of the brain by the hemorrhage causes a certain amount of brain compression, and a greater functional disturbance than is caused by a simple obliteration of the artery's lumen. Surgical experience seems to confirm also the fact that brain lacerations are attended by rise of temperature. Thus, Dr. Charles H. Phelps has called attention to the great uniformity of elevated temperatures in injuries to the head, attended with contusion or laceration of the cortex. He thinks that there is sometimes an initial fall of temperature, followed by a progressive rise, and that this rise is a more constant symptom than unconsciousness. In 83 cases, of which in 45 there was an autopsy, this elevation of temperature was noted. He thinks it due to injury to the cortex, but does not place it in relation with any special portion of the cortex or to any heat-centre.[1]

[1] New York Medical Journal, January 14, 21, and 28, 1893.

I append here the histories, much condensed, and the charts of the cases illustrating the temperature changes to which I have referred. I might add at this point one word with regard to the preliminary sudden fall of the temperature in cases of apoplexy. This preliminary fall is certainly a thing of rare occurrence. In my own experience I have seen it only once, and in looking over records of nearly two hundred cases of apoplexy due to hemorrhage or softening, the report of a preliminary temperature fall was not made. This, to be sure, may be explained on the ground that most of our hospital cases and many of our private cases are not seen until some hours after the shock occurs. I can only say, therefore, that practically it is a phenomenon rarely observed, and as I have seen it occur both in embolism and in hemorrhage, it has not a very great diagnostic value; still it undoubtedly does occur at times, and it occurs more frequently with hemorrhage than with softening.

CASES OF CEREBRAL HEMORRHAGE.

Case I.—Julius Z., aged sixty years, admitted to hospital, January 17th; no previous history. Patient completely unconscious, breathing heavily; pupils even and moderately contracted. Total motor paralysis of right side, with well-marked anæsthesia of face and arm, less marked of trunk and leg. Heart and urine normal. Next day stupor not so extreme, occasionally speaks; anæsthesia less; paralysis the same. The next three days patient continued about the same. Death on the sixth day. Temperature as indicated in Case I.

Autopsy. Lungs normal; heart normal. Extensive cerebral hemorrhage in left cerebrum between optic thalamus and left lenticular nucleus, involving the thalamus, extending into the left lateral ventricle and somewhat into the right. Small clot in fourth ventricle from passage of blood through aqueduct of Sylvius.

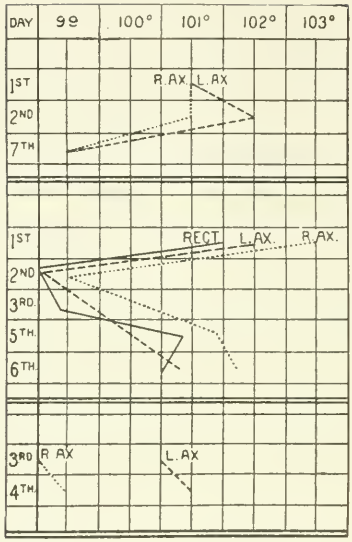
Case II.—Female, aged sixty-eight years; admitted in a semi-comatose state with right hemiplegia and anæsthesia. She died on the third day. The temperature ranged continuously, 98½° to 99½° and 100°, and was a degree higher on the paralyzed side.

Autopsy showed a large clot on the convexity of the left hemisphere. (Details given in the *Medical Record*, 1887, p. 280.)

Case III.—The patient was a woman, aged thirty-eight years, who was admitted with hemiplegia and coma. She lived nine days, gradually rising and showing the differences on the third and fourth days, indicated by the chart.

Autopsy showed a clot in the left temporal lobe and left ventricle.

CHART I.



Unilateral temperature in cerebral hemorrhage.

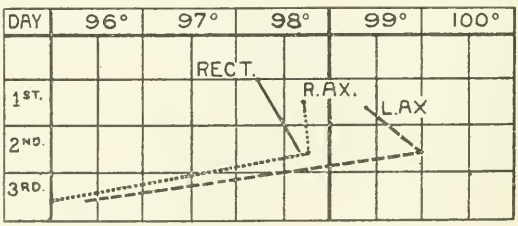
CASE IV.—Male, aged seventy years. Fell down suddenly with right hemiplegia, later became unconscious. Next day brought to Bellevue Hospital (August 18th). Unconscious, hemiplegia of right side; pulse 72, and full. "Skin warm on right side, cold on left." Temperature 99½°. Died on second day.

Autopsy showed hemorrhage involving the left corpus striatum and optic thalamus and breaking into ventricles. Beginning hepatization of lungs.

CASES OF ACUTE SOFTENING.

CASE V.—Leonardo L., aged forty-four years, brought to hospital June 4th; was partly conscious and spoke a few words; soon lapsed into semi-

CHART II.



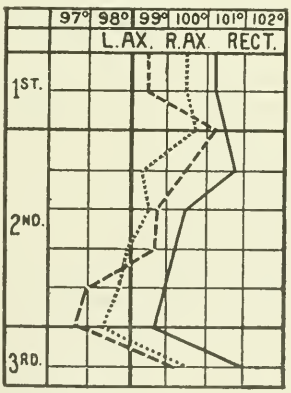
conscious condition from which he could be roused with difficulty. Total paralysis of left side, with diminished reflexes. Pupils equal, respond slug-

gishly; analgesia of left side, as shown by pricking with needles. Patient continued in semi-conscious condition, and died on third day. Temperature as indicated in Chart II.

Autopsy. Brain showed a softening about the hippocampus major of right side; the area of softening extended into the central white matter of the occipital lobe and forward into the temporo-sphenoidal lobe. The hippocampal convolution and gyrus fornicatus were not involved, but the area of softening was such as might include fibres from these parts. The basal ganglia were not involved; pons and medulla normal.

Case VI.—Peter J., aged fifty-nine years; syphilis twenty-four years previously. Heavy drinker. Patient felt well up to previous night when he retired. Next morning, on arising, felt a numbness and weakness in left side. Was brought to the hospital next day. There is fine tremor and some ataxia in both arms; ataxia more marked on left side. Marked loss of power in left hand and leg, with exaggeration of deep reflexes. Urine normal. Intelligence fairly good at first, but patient gradually became semi-conscious and delirious, and died November 22d, twenty-two days after admission. No temperature records were made between November 4th and 16th. The temperature in the rectum from the day after admission up to November 4th ranged from 99½° to 97⅘°, there being no marked variations. On the second day it was 98½°, on the tenth day 98°. On the fourteenth day temperatures were taken in right and left axillæ, giving records such as are shown in Chart III.

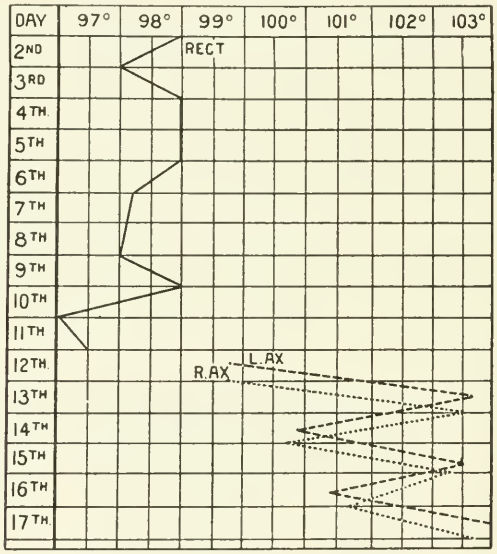
Chart III.



Case VII.—John B., aged seventy-three years, German, was admitted to the hospital March 9th in a condition of coma. No history. The patient can be partly roused to a consciousness of his surroundings. Face flushed; breathing quiet. Head and eyes turned to the right. Pupils moderately dilated and even. Marked rigidity of all the limbs, most pronounced in the left arm. The left hand and fingers are held rigid, the fingers being

flexed. Heart-action weak. Slight amount of albumin in the urine. Twenty-four hours after admission the patient had slight spasms, beginning with convulsive movements of the face and left hand. The patient was bled seven and one-half ounces from the arm, and seemed more conscious on the second day. The record shows that after this the stupor gradually deepened, and the patient became comatose, dying early the third day. The temperature record of the three days that he was in the hospital was taken in each axilla and in the rectum, and is indicated in Chart IV.

Chart IV.



Post-mortem showed in the brain two spots of softening, involving symmetrically each lenticular nucleus, and more particularly the globus pallidus.

This case I shall refer to again, because of its interest in connection with heat-centres. The temperature, as will be seen, did not rise in the axilla above 100.2°, and was most of the time normal. The rectal temperature showed a slight rise only. The temperature was taken very carefully eight times during the three days of the patient's presence in the hospital.

Case VIII.—Thomas P., aged forty years, had suffered from locomotor ataxia for ten years; was still in the walking stage. Had a history of syphilis fifteen years before. Had a severe valvular heart lesion with hypertrophy. Sudden complete left hemiplegia, with inability to articulate or swallow except with great difficulty. The paralysis was almost total of

arm and leg. The patient was semi-conscious and at times delirious. No anæsthesia. He improved slightly for four days, then grew worse and died on the eighth day. His temperature was taken in the axillæ three or four times a day during this whole period. The temperature in the first twenty-four hours ranged in each axilla from 100° to 101°, being equal on the two sides. It fell a little below 100° on the second day, and continued at about 100° until the day before death, when it sank in each side to 98° or 99°; at one period it fell as low as 96.4°. The record is shown in the table.

Temperature in Case VIII.

Time.	Right axilla.	Left axilla.
January 28, 1890.		
7.00 A.M.	100	$100\frac{4}{5}$
12.20 P.M.	$100\frac{1}{5}$	$100\frac{3}{5}$
7.15 "	102	$101\frac{3}{5}$
January 29. (Third day.)		
7.30 A.M.	99	$99\frac{1}{5}$
2.45 P.M.	$99\frac{4}{5}$	$100\frac{2}{5}$
7.15 "	$100\frac{4}{5}$	$100\frac{4}{5}$
January 30.		
7.00 A.M.	99	$98\frac{3}{4}$
12.00 M.	$99\frac{4}{5}$	$99\frac{3}{5}$
7.00 P.M.	$101\frac{2}{5}$	101
January 31.		
7.00 A.M.	$100\frac{2}{5}$	$100\frac{1}{5}$
12.15 A.M.	101	101
8.00 "	100	$100\frac{4}{5}$
February 1,		
8.00 A.M.	99	$99\frac{4}{5}$
12.30 P.M.	$99\frac{2}{5}$	99
7.00 "	$100\frac{3}{5}$	101
February 2.		
8.30 A.M.	$97\frac{4}{5}$	$98\frac{4}{5}$
1.45 P.M.	98	99
7.00 "	100	100
February 3.		
12.30 A.M.	98	99
8.00 "	$96\frac{2}{5}$	$96\frac{4}{5}$
12.00 M.	$96\frac{4}{5}$	98

The *autopsy* showed a large embolus blocking up the right middle cerebral artery, and causing an area of softening, involving the internal capsule and corpus striatum, some of the optic thalamus and centrum ovale. The heart showed serious valvular lesions as well as hypertrophy.

Case IX.—Ann G. Sudden right hemiplegia with motor aphasia, dysphagia, right hemianæsthesia very marked in the face. Intelligence dull. Early rigidity of paralyzed side; progressive weakness; death in two months. This patient, whose history I have detailed in my article on "The Cortical Localization of Cutaneous Sensations," showed a continuous slight difference of temperature of the two sides, amounting for a time to a degree or more, and in particular an initial fall of temperature on the non-paralyzed side during the first two days. There was, however, at no time any marked rise of temperature on either side, the range being 98.5° to 99.5°.

The *autopsy* showed atheromatous arteries and a large patch of yellow softening, involving the second and third left frontal and part of the lower half of the precentral convolution of the left side.

Case X.—A woman, aged sixty years; left hemiplegia; death on the fifth day. Temperature on the fifth day in each axilla 98.5°.

The *autopsy* showed thrombosis of the right middle cerebral.

The clinical and pathological facts which I have collected and presented here do not, as a matter of fact, represent all the evidence which I possess to sustain the view that hemorrhages cause in the first place a greater immediate rise of temperature, and in the second place a greater unilateral difference in temperature than softenings do. One must bring to bear upon the judgment of such questions personal experience in cases where the positive pathological data are not obtainable, as well as the experience of other observers; and it is with a full consideration of these facts in mind that I have reached the conclusions which I have stated.

We come now to the third question, that is, as to the effect of the *special localization of clots or softened spots upon temperature changes*, and this question brings up at once the whole subject of thermic centres.

The experimental investigations made for the purpose of discovering heat-centres have been numerous, and it is not my purpose to go into this subject extensively. The work of Ott,[1] Wood,[2] and Reichert[3] in this country, of Hale White[4] in England, of Aronsohn and Sachs,[5] Landois, Eulenberg, Girard,[6] Baginsky and Lehmann,[7] and Baculo[8] on the Continent, has produced results which are somewhat conflicting.

Some experimenters have found that injuries of the caudate nuclei and corpora striata produce a rise of temperature. Ott finds a rise of temperature resulting from a puncture just in front of the caudate nuclei, but lays especial stress upon the tuber cinereum as a heat-centre. Reichert finds (1) that the automatic thermogenic centres are located in the spinal cord; (2) that the cruciate and Sylvian centres are thermo-inhibitory; (3) that the caudate nuclei and medulla oblongata contain thermo-accelerator centres; (4) that no specific heat centres probably exist in the optic thalami; (5) that specific thermotaxic heat-centres, *i. e.*, centres having a common control over both heat production and heat dissipation, do not exist.

[1] Therapeutic Gazette, September, 1887; Journal of Nervous Diseases, April, 1894.
[2] Smithsonian Contributions: Fever.
[3] University Medical Magazine, March, 1893, and 1894, p. 303.
[4] Journal of Physiology, 1891, vol. xii. p. 233.
[5] Pflüger's Archiv f. Physiol., lvi. p. 237.
[6] Archiv de Physiol., 1886, viii. p. 28.
[7] Virchow's Archiv, 1886, cvi. p. 258.
[8] Journal of Nervous and Mental Diseases, March, 1891.

Nearly all observers find that lesions of the corpus striatum are followed by marked increase of temperature, generally due to increased heat production. Baculo believes that the thalami are heat-centres, but both Reichert and White seem to doubt this. In some experiments of Wood and White lesions of the crura cerebri were followed by febrile rise, but Reichert does not confirm this. Nearly all experimenters agree that lesions of the pons cause a rise in temperature. White thinks that lesions of certain points of the cerebral cortex may cause a rise of temperature and also lesions of the crura cerebri and of the septum lucidum.

About all that one can conclude from the physiological experiments thus briefly referred to is that injuries of the corpus striatum and of the pons cause a rise of temperature. As to whether injuries of the tuber cinereum or optic thalamus or cortex have a similar effect the evidence is still conflicting. It seems to be pretty well agreed that injuries of the cerebellum and of the white matter and frontal and occipital lobes of the cerebrum do not cause temperature elevations.

The question arises now whether these somewhat conflicting physiological data can be applied to clinical medicine. Dr. Hale White has endeavored to fulfil the task of making this application, and in the various articles which he has written[1] has reported cases of his own and of others which lead him to think that there are thermic centres in the brain. He reports cases in which lesions of the corpus striatum were followed by rise of temperature; also cases of lesion of the cortex and of the pons with similar phenomena. His cases, however, do not, in my opinion, stand close critical analysis. In Casé II., for example, which is cited as an illustration of lesion of the corpus striatum with fever, the hemorrhage extended into the right and third ventricle. In Case VIII. his patient, a boy of six and a half years, had right hemiplegia for three months before any fever came on; then he had convulsions. Autopsy showed a double lesion of the corpora striata. In another case[2] a man had paraplegia for a year before fever came on. Autopsy showed a bilateral softening of both internal capsules, involving slightly both the striata

[1] Guy's Hospital Reports, vol. xxvii., 1884; Lancet, June, 1891, and September, 1893. International Clinics, 1893, p. 163.

[2] Lancet, June 29, 1891.

and the thalami. He quotes a case of Ollivier in which there was a hemorrhage into the optic thalamus and crura cerebri with a temperature of 102°, and another case of hemorrhage into both optic thalami with a temperature of 105.7°;[1] also a case of Wernicke's of hemorrhage into the basic ganglia with a temperature of 105°;[2] and one of Bourneville's of hemorrhage into the optic thalamus, ventricle, and corpus striatum with temperatures of 103.4° and 107.6°.[3] Another case supposed to be in point is one reported by Bagojawlewski, of echinococcus of the corpus striatum with rise of temperature.[4] All these cases, however sympathetically considered, seem to me to carry but slight weight, for, in the first place, very few of them are strictly localized lesions; in the next place, as I have already shown, sudden lacerating lesions, like that of hemorrhage, will, if of any extent, cause rise of temperature, no matter where located, as a rule; and, finally, there are cases of localized lesions of these supposed thermic centres in which no hemorrhage has been found. I have myself reported above a case of bilateral lesion of the striatum without any fever, and I have the records of a similar case with similar absence of temperature rise. I have no doubt that a diligent search of records would lead to the accumulation of a great deal more negative evidence.

With regard to lesions of the pons, however, there is more uniform agreement. Undoubtedly a lesion of the pons, unless very small, will cause immediately a rise of temperature. As for lesions of the cortex, it is the opinion of Dr. Phelps that contusions of this region, wherever they occur, are almost uniformly associated with rise of temperature; and he is inclined to believe that this rise is dependent, not upon the point of location of the lesion, but upon its character. Surgeons who operate upon children are familiar with the sudden shooting up of the temperature for twenty-four hours after a linear craniectomy, and this rise is, perhaps, due to some temporary injury of the cortex.

My own cases bearing on thermic localization are—some of them —of much interest. Thus in Case VI., Peter J., above referred to, the temperature ranged never above 99° until the twenty-first

[1] Gazette Hebdomadaire, 1875, No. 12.
[2] Lehrbuch der Gehirnkrankheiten, ii. 48.
[3] Etude clin. et thermomét. sur les Maladies du Système Nerveux.
[4] Centralblatt f. d. med. Wissenschaften, 1888.

day; then it gradually rose to 100° and 104°, as shown in chart. The autopsy record reads: "On the outer edge of the right lenticular nucleus there was a patch of softening about the size of a bean. There were also many capillary extravasations in the lenticular nucleus and in the adjoining internal capsule." The lungs were practically normal. Left brain normal. This case might be used by the localists, but the lesion was present for three weeks before the fever. In Case VII., above cited, there was a double softening of the lenticular nucleus, and here the temperature rose on one day to 101.8° in the rectum, but its general average was but slightly above normal. I have another case of localized clot in the lenticular nucleus. The patient had hemiplegia, but gradually improved. A few weeks later she developed pneumonia and died. Temperature records are given as soon as the pneumonia appeared, and I can only infer that, according to custom, it was taken at first, found normal, and then not recorded. Cases of complete blocking of the middle cerebral with hemiplegia due to softening, involving the corpus striatum, without fever, are, I believe, not uncommon. Case X. illustrates one of this class. My cases illustrating lesions of the thalamus and neighboring parts are also of interest.

Case XI. is that of a man aged sixty-four years, who was admitted with left hemiplegia and hemianæsthesia and dulled intelligence. He became somewhat delirious and died on the seventeenth day, eight weeks after his attack. During the last four days of his illness the temperature ranged from 97.6° to 98°.

Autopsy showed an old hemorrhage occupying the site of the right optic thalamus. On the outer side of the old hemorrhage is a more recent one. Here is a *clot in the optic thalamus with subnormal temperature.*

Case XII. is that of a man admitted to the alcoholic cells with delirium tremens and a temperature of 105°. He died on the third day with a temperature of 105.8°.

Autopsy showed a clot the size of a bean in the middle of the right optic thalamus; brain intensely congested; lungs normal. Here, however, the febrile disturbance might have been due to alcoholism.

Case XIII. may have some interest in connection with Dr. Ott's theory that the tuber cinereum is a thermic centre. The patient was a woman of fifty years, who came into the hospital in a semi-delirious state. She had small rigid pupils and slight right hemianæsthesia. She continued nearly comatose for eight days, and died of œdema of the lungs. Temperature on admission, 102°. It ranged between 100° and 102° until she died.

Autopsy showed "softening of the inter-peduncular space;" the walls of the third ventricle, and the optic thalami on each side, were slightly softened. The corpora quadrigemina were slightly affected.

I have records of a case of softening of the frontal lobes with normal temperature, and one of hemorrhage into one frontal lobe with a temperature of 102°. But my paper has already exceeded its limits.

It is a fact of some importance, and one to be borne in mind in estimating the value of experiments on animals, that the regions which cause temperature rise are also those which are most vascular, and lacerations of such parts must necessarily have a greater traumatic importance. Then again, the transference of the results of animal experiments to man involves a good many elements of error. The corpus striatum of the rabbit, for example, is a very important part in that animal's brain; but in man this ganglion is a latent region and is probably a rudimentary organ, a vestigium, whose original work has been transferred to the brain cortex. Man gets along very well with badly injured striata, but the rabbit does not, and heat-centres in this latter animal would not have necessarily the same locus in man.

In two cases where the optic thalamus was especially involved in hemorrhage there was a very high temperature, but in almost all my cases the high rises of temperature were associated with extensive lacerating lesions or else with some superimposed inflammatory process in the lungs. This latter fact must always be borne in mind in reporting cases of apoplexy with subsequent fever. Very often a sharp rise of temperature in three or four days after a stroke indicates only a beginning pneumonia, and in two of my cases I have found the pneumonic process to be fetid in character and accompanied naturally with a very high fever.

Taking all the facts into consideration, it seems to me that we cannot yet assert that there are any definite heat-centres in the human brain, and can only say that temperature rises are more apt to be caused in man by lesions of the pons than elsewhere, and next to this by lesions of a hemorrhagic and lacerating kind, involving the cortex cerebri.

Allow me now, gentlemen, in conclusion, to review the results which I have endeavored to reach. They are :

1. That all intra-cranial hemorrhages, whatever their location, are much more apt to be accompanied with immediate disturbances of temperature than are necrotic processes from embolism and thrombosis. These temperature disturbances in hemorrhages are, in rare cases, a sudden initial fall; then in almost all cases except where the lesion is small, there is within a day or two a rise of temperature of from one to three degrees. On the other hand, in acute softening this initial fall and early rise do not occur unless the process is very extensive or involves the pons.

2 In apoplexy due to hemorrhage, the temperature is greater upon the paralyzed side than on the normal, the difference averaging about one degree. In acute softening this unilateral difference of temperature does not occur or is extremely slight.

3. The rise of temperature due to apoplectic lesions depends more upon the extent and nature of the lesion than upon its location. Lesions of a traumatic character in the cortex, however, are especially apt to cause a rise of temperature. Lesions in the pons also either of hemorrhagic or softening character, almost uniformly cause a rise of temperature unless quite small.

4. There is as yet no clinical evidence that lesions of the basal ganglia or the parts about them cause temperature rises on account of destruction of certain thermic centres; in other words, the clinical and pathological evidence of thermic centres in the human brain, aside from the parts mentioned, is yet inadequate.

5. Finally, gentlemen, I would specially impress upon you the great value, from a diagnostic point of view, of a careful study of the temperature changes after apoplectic strokes. The temperature should be observed on each side of the body, in the rectum also, if possible. With data thus obtained one can, I feel sure, gain much more positive evidence as to the nature of the lesion in these cases, and I have repeatedly been able to satisfy myself, in my clinical work, of the nature of the lesion by means of the methods referred to. I do not believe that with the help of the numerous factors which we now have in aiding our diagnosis there are many cases of apoplexy in which it is difficult to make a diagnosis. The old-time tabulation of differential points in diagnosis between hemorrhage and acute softening still remains of value. We need, and must use, all the helps possible; but if we, in addition to other methods, care-

fully apply the thermometric, I am sure we can reach vastly more satisfactory results.

Previous Papers on Apoplexy by the Author.

"Forms of Cerebral Hemorrhage." *Medical Record*, August, 1890.

"Diagnosis of Intra-cranial Hemorrhage and Acute Softening," *Medical Record*, July 25, 1891.

"Vertigo in Temporal Lobe Lesions." "Cerebral Abscess with Hemorrhage." *Journal of Nervous and Mental Diseases*, July, 1889.

"Primary Hemorrhage in Lateral Ventricle." *Journal of Nervous and Mental Diseases*, 1892, p. 47.

"The Apoplectic Pulse." The *Post-Graduate*, 1893, p. 276.

DISCUSSION.

Dr. J. J. Putnam: I am unwilling that Dr. Dana's valuable contribution should go without some comment, if it is only to say how much we appreciate it. All I can add for my own part, is one case of probable hemorrhage (although there was no autopsy) in which the temperature taken in the axilla did go up very much higher on the affected side than on the opposite side.

Dr. C. G. Stockton: I would like to inquire of Dr. Dana in what manner the temperature was taken. Does he mean by "temperature on the affected side," the temperature taken over the lesion in the brain or in the axilla?

Dr. Dana: I did not read all the details of my paper, or this point would be clear. I mean to say that the temperature in the axilla on the affected side is greater than on the non-paralyzed side. My instructions to the attendants is to have the temperature taken in each axilla and in the rectum every three hours during the first few days of the attack.

THE FREQUENCY OF RENAL ALBUMINURIA, AS SHOWN BY ALBUMIN AND CASTS, APART FROM BRIGHT'S DISEASE, FEVER, OR OBVIOUS CAUSE OF RENAL IRRITATION.

By FREDERICK C. SHATTUCK, M.D.,
OF BOSTON.

In no branch of human activity, perhaps, can more striking illustrations be found of the dangers of hasty conclusions from insufficient data than in medicine. This is no reflection on our calling. It naturally flows from the fact that our knowledge of many things is still very imperfect, while the demands for the practical application of our knowledge are constant and imperative. The sick man wants instant help, and cannot wait while doubtful points are being settled. Medicine is more than an art; less, in a sense, than an exact science. The clinical significance of albumin and casts affords one of these illustrations. The chemical preceded the microscopical examination of the urine, and the latter first made it possible to determine with any accuracy the portion of the urinary tract from which the albumin is derived. The presence of casts shows that the true renal tissue is involved, and was for some time held to be diagnostic of Bright's disease. I well remember the grave prognosis which the discovery of albumin and casts was thought to necessitate when I was a hospital interne, not much more than twenty years ago. Perhaps I incorrectly interpreted my teaching—students sometimes do—but I think this was at that time generally regarded by the profession as damning evidence. Albumin and casts meant Bright's disease, and that meant an inevitably and more or less rapidly fatal disease.

Further experience and the irresistible logic of facts have led to

such changes in these views that considerable discussion has been held as to whether albuminuria may not be physiological, so common is it found to be, so little bearing may it have on the vigor or longevity of its possessor. Into this discussion I do not propose really to enter. Absolute physical perfection is occasionally found in the human being; but the ideal and the real are nearly as sharply contrasted in the more purely bodily as in the moral qualities. Whether there be a physiological albuminuria is largely a matter of definition of the word physiological.

Much ingenuity has been devoted to the discovery and application of tests of extreme delicacy for albumin. My friend and colleague, E. S. Wood, assures me that for clinical and qualitative purposes, none of these tests can compare with the old heat and nitric acid tests, and I am glad to see similar views expressed very recently by D. D. Stewart,[1] of Philadelphia. These are the tests used in the cases which I have analyzed. A cloudiness of the boiled upper layer of urine in the test-tube after the addition of acetic acid, and the opaque zone with nitric acid are therefore considered proof positive of the presence of albumin, as a negative result is proof of its absence. To my eye the heat test is the more delicate of the two, but I know that all do not find it so. Vanderpool,[2] in a recent paper on albuminuria without manifest organic renal lesion, has collected the literature of the subject, and justly calls attention to the discrepancy which exists between the percentages of different observers examining considerable numbers of presumably healthy persons. Chateaubourg finds albuminuria in 84 per cent. of 701 examined; Grainger Stewart, in 31 per cent. of 407 examined. Others put the percentage still lower, but even this discrepancy is sufficient to show that something is the matter. Doubtless Millard is right in believing that Chateaubourg, who used Tanret's test in many of his examinations, mistook mucin, or some other non-albuminous organic substance, for albumin. As far as I know, casts have not been looked for as carefully as albumin. The search for them demands a good deal of time if the sediment is scanty; and they may easily be overlooked when present, if ample time is not allowed the urine to settle, and if skill in the selection of portions of the

[1] The Medical News, May 5, 1894.
[2] Medical Record, November 11, 1893.

sediment is not exercised. Experience has led me to be skeptical when the statement is made to me that a distinct trace of albumin is present, but that casts as well as other formed elements, such as blood and pus, are absent. In such cases I have repeatedly found that more careful examination revealed the casts. These bodies still enjoy a worse reputation in the minds of the laity than albumin, as well as in the minds of the profession in general. Patients are alarmed by the knowledge that there are casts in their urine, much as they used to be by hearing that they had a murmur in their hearts.

For five or six years now I have been more and more particular to have a thorough examination of the urines of patients seeking my advice made by competent men, quite irrespective of the nature of the complaint which brought the patient. The frequency with which albumin and casts, chiefly hyaline and finely granular of small diameter, were reported in those at or beyond middle life, entirely apart from any other evidence of renal mischief, attracted my attention. This led to the preservation of the reports of those of fifty years of age or more, and more recently also of the younger patients. Consequently, I deal with larger figures relatively, or absolutely at the later ages. I now regret that I did not begin my collection on a more comprehensive basis. All the same, it does not seem probable that the result would be very materially modified. In the decade of twenty to thirty I believe that a larger number of cases would reduce the percentage of those with renal albuminuria, and I think also that larger figures would show the condition to be quite as frequent between eighty and ninety as between seventy and eighty, but I cannot regard these sources of error as serious.

In the collection of these cases I have excluded all those with fever; all in which such well-known renal irritants as bile and sugar were present, no matter how small in amount; and also those in which examination rendered it probable that the mechanical effect of crystalline formation in the kidneys was directly responsible for the albumin and casts.

In the division of cases reported as showing albumin and no casts, no cases are included in which there was sufficient blood or pus, either from the vagina or lower urinary passages, to account for the reaction. In many of these I am convinced that more care-

ful search would have revealed casts. Cases of cardiac and other organic disease are included, but I have tried to omit all those in which passive congestion could account for the findings. Of course, all cases of unquestioned Bright's disease are excluded. In short, the attempt has been made to determine approximately how frequently renal albuminuria and casts are encountered in the urine in the ordinary run of adults who consult a doctor, but present no evidence outside of the urine, of primary or secondary renal disease. Some sixty of the patients were hospital cases, partly medical, partly surgical, suffering from widely varying maladies or injuries. No record has been kept as to the time at which the urines of my cases were voided. The larger number probably were passed on rising in the morning, many were passed at mid-day in my office, some both morning and evening, and not a few were mixed specimens of the twenty-four hours.

The personal equation can be eliminated from my results for the reason that the examination was made in, roughly speaking, nearly equal proportion by four different observers, and a few by two others, all competent to distinguish mucous from renal casts. The small percentage of cases in which albumin was found without casts shows, I think, that no serious suspicion can attach to my results on the ground that other substances were often mistaken for albumin. In the great majority of cases but a single examination was made, but in a fair number there were two or more.

Age.	No. of cases.	Albumin and casts.	Per cent.	Albumin and no casts.	Per cent.	No albumin or casts.	Per cent.
20 to 30 . .	25	8	32	3	12	14	56
30 " 40 . .	39	9	23	4	10	26	66
40 " 50 . .	47	26	55	3	6	18	38
50 " 60 . .	99	64	65	11	11	24	24
60 " 70 . .	57	42	74	5	9	10	17
70 " 80 . .	16	16	100	0	0	0	0
80 " 90 . .	14	11	79	0	0	3	21
	297	176	59	26	9	95	32

This table needs little explanation. It shows that the percentage of urines containing albumin and casts rises steadily with each

decade from the fourth to the eighth, while those free from albumin and casts are in steadily decreasing percentage, and the proportion of those containing albumin but no casts remains nearly the same throughout. The number of cases in which casts were found without albumin was so small that they have not been classified.

The question remains as to the significance of these results. The pathological meaning is not easy of absolute proof. The class of patients who form the basis of my statistics are slow to die, and office and hospital patients are easily lost sight of. A considerable number of the patients I know to be alive, and apparently as well as when albumin and casts were discovered a number of years ago. In only two have I notes of autopsies. In one patient of eighty-five death was the result mainly of old age, and the kidneys were exceptionally healthy to the naked eye. In another of eighty-six death was due to sudden uræmia supervening on prostatic enlargement, necessitating repeated catheterization; cystitis, and impacted calculus at the vesical end of the left ureter; the kidneys were cystic and atrophic, especially in the cortices. Albumin and casts were found four years before death, and yet the general health was remarkably good for a person of upward of eighty years. In some of the cases albumin and casts were undoubtedly due to active hyperæmia, or to irritation of the kidneys, and was perhaps transitory; but it is my belief that the facts in my table are best explained on the theory that the albumin and casts are the expression of senile renal atrophy, especially as far as the higher decades go.

There is no internal organ in which it lies in our power to detect so unerringly minute and slight changes as in the kidney. The heart, lungs, and bloodvessels, as a whole, are far less accessible to our examination. Age is not a matter of years, nor do we grow old symmetrically. I see no other reasonable explanation for the progressive increase in the frequency of albumin and casts as age advances. Whether this pathological doctrine be true or not, the clinical significance admits, to my mind at least, of no doubtful interpretation. My anxiety is not awakened either for the present or the future by the report that a faint trace of albumin and hyaline and finely granular casts of small diameter are found in the urine of a patient after the age of fifty, provided that the kidneys are

doing sufficient work, as shown by the twenty-four-hour excretion of solids, and provided there are no symptoms.

Three years ago I was consulted by two brothers, fifty-two and fifty-five years of age, who had been urgently solicited to take out life insurance policies for one hundred thousand dollars each. But the ardor of the company was cooled when it was found that their urines contained a slight trace of albumin and casts, and their anxieties were awakened. Albumin and casts were constantly found in several examinations during the succeeding year; but the men were, and remain, perfectly well. The urines were rather concentrated. In patients under fifty albumin and casts do not disturb me anything like as much as they did formerly. The important practical point is that they are not necessarily the precursors of serious kidney disease, and that their presence does not inevitably demand very careful regulation of the life and constant medical supervision.

In a certain proportion of cases, how large this proportion may be it will take years to determine, interstitial changes will reach a degree to shorten life, advancing more or less rapidly. It is not in our power at present to distinguish accurately which these cases are. Some help is afforded by the close estimation of solids in the twenty-four-hour urine; but in the average individual the reserve balance of kidney power is sufficient to permit of extensive renal impairment without curtailment of the ordinary daily work. The reserve may be diminished or gone; but if the reserve is not drawn upon too much or at all no apparent stringency is felt. We can grant that renal albuminuria is always pathological. Chronic pharyngitis is also pathological. It may be heresy, but I cannot resist the feeling that we are coming to believe that the clinical significance of the one is not necessarily greater than that of the other. I shall follow up my cases as far as I can, and hope to be able in the course of years to throw further light on this important practical question. Life insurance companies are right in refusing risks reported as presenting albumin and casts. Life insurance is more like the French than the English criminal law—it holds that innocence must be proved beyond reasonable doubt. But I have no question that risks are daily accepted by the best companies where an expert examination would detect albumin and casts. Few examiners apply

the heat and nitric acid tests in a manner to try their full delicacy, and a microscopical examination is practically not demanded. Even if it were, it would not ordinarily be sufficiently careful to be of much value.

Finally, my results may be summed up in the following conclusions:

1. Renal albuminuria, as proved by the presence of both albumin and casts, is much more common in adults quite apart from Bright's disease or any obvious source of renal irritation than is generally supposed.

2. The frequency increases steadily and progressively with advancing age.

3. This increase with age suggests the explanation that the albuminuria is often an indication of senile degeneration.

4. Though it cannot be regarded as yet as absolutely proved, it is highly probably that faint traces of albumin and hyaline and finely granular casts of small diameter are often, especially in those past fifty years of age, of little or no practical importance.

DISCUSSION.

Dr. I. N. Danforth: My own observations have closely followed those of Dr. Shattuck for several years past. It is perhaps twenty years ago now, that a patient came to me who had albuminuria and casts. At that time I did not know so much about the subject as I do now, and yet there is plenty of room for me to learn. I remember that I told him that he had Bright's disease, that he had not long to live, and that he had better make arrangements for a change of worlds. That man is still alive and still as well as he was then, and attending to his vocation. This is an example of many cases that I have seen. I have come to regard transitory albuminuria of slight amount as a small matter, and the presence of casts, provided they are small, symmetrical, hyaline casts, as not necessarily involving any special danger. Nevertheless, I insist that the character of the casts determines the real condition of the kidney; and I insist, also, that a study of the structure of the casts requires a great deal more study and observation. I have contributed a little in that direction to the records of this Association and have some work partly finished, which I propose to submit later.

EXPERIMENTAL PHTHISIS IN RABBITS WITH THE FORMATION OF CAVITIES—A DEMONSTRATION.

By T. M. PRUDDEN, M.D.,
OF NEW YORK.

It is well known to the members of this Association that attention has for some time been turned to the concurrent infection of the lungs in pulmonary tuberculosis with other germs, such as the streptococcus pyogenes, micrococcus lanceolatus, staphylococcus pyogenes, etc.

Sufficient data are at hand to justify the conviction that this secondary infection often plays an important rôle in determining the symptoms and lesions of pulmonary tuberculosis.

As a part of a series of studies on this subject, carried on during the past winter, I undertook to find out, among other things, the effects in rabbits—already the subjects of an extensive experimental pulmonary tuberculosis—of intra-pulmonary injections through the trachea of beef-tea cultures of the streptococcus pyogenes.

The streptococcus pyogenes alone introduced through the trachea into the lungs of healthy rabbits usually induces a slight temporary localized bronchitis and a moderate proliferation of vesicular epithelium. These small inflammatory foci usually soon disappear without serious interference with the health of the animal.

The tubercle bacillus alone, introduced in considerable quantity through the trachea of healthy rabbits, is capable of causing large areas of tubercular consolidation of the lungs, with varying amounts of cheesy degeneration. This experimental lesion of the rabbit's lung, caused by the tubercle bacillus alone, is closely similar to certain phases of cheesy pneumonia or acute phthisis, as we see it in man, save that in the animal lesion cavities are not apt to form.

Now in my experiments, one of whose results I wish to illustrate by this demonstration, having established the separate effects upon the rabbit's lung of the streptococcus and of the tubercle bacillus, I introduced the streptococcus into lungs already the seat, for varying periods, of extensive tubercular lesions.

The result of this secondary concurrent infection was not, as had been deemed possible or probable, an increased amount of exudative pneumonia nor a hastening of the death of the animals, but a more or less extensive formation of cavities in the affected portions of the lungs. This formation of cavities occurred in eight out of nine lungs subjected to the conditions of this experiment, whereas in only one lung out of eleven did cavities form under the influence of the tubercle bacillus alone.

My demonstration consists in the exhibition of photographs of the lungs of these rabbits, both with the simple and the mixed infection, and of some of the lungs themselves.

I am not prepared, in this preliminary communication on these studies, to consider the significance of these rather striking results. It has often been said, in reproach, that experimental pulmonary tuberculosis has failed to throw light on one of the more important phases of phthisis in man, because the development of cavities in animal lungs has hitherto been of the most infrequent and uncertain occurrence.

Whatever the full significance and practical bearings of these studies may prove to be, these specimens show, I think at least, and this is all I want to show now, that pulmonary phthisis, cavities and all, can be experimentally induced in the lower animals.

A REPORT OF THE ULTIMATE RESULTS OBTAINED IN EXPERIMENTAL EYE TUBERCULOSIS BY TUBERCULIN TREATMENT AND ANTI-TUBERCULAR INOCULATION.

By E. L. TRUDEAU, M.D.,
OF SARANAC LAKE, N. Y.

At the last two meetings of the Association I presented rabbits, illustrating the beneficial influence which may result from tuberculin treatment in experimental eye tuberculosis, and the marked inhibitory action exercised over this type of disease by preventive inoculations. In a morbid process, however, following so irregular a course, and of so relapsing a nature as tuberculosis, time must ever be the crucial test which should be applied to any apparently favorable results obtained, and I therefore report briefly the further results of these experiments.

The curative effects of tuberculin on the eye lesions, which, as I showed, may go on apparently to absolute disappearance of the tubercular process in the eye, is in but very rare instances permanent, and a strong tendency to relapse sooner or later becomes apparent. Even after the eyes have remained free from any morbid manifestation as long as twelve months will this tendency to recurrence manifest itself. Little by little signs of vascular irritation appear in the eye and around the remaining trifling and apparently extinct foci, and these slowly show evidence of renewed activity. The course of the relapse in the great majority of cases, however, seems essentially chronic, and the destructive and inflammatory processes resulting in caseation are less marked than those which occur after the primary inoculation.

The tendency to recurrence after tuberculin treatment exists, therefore, though to a much less degree, experimentally as clinically,

and the extent to which the tubercular process can be influenced favorably seems to depend rather upon the degree and character of the irritation induced about the tubercle, and the length of time which this irritation can be maintained as a result of the treatment, than upon any direct germicidal effect or upon the production of a lasting immunity. In lupus we note that the manifest and marked good effects of the treatment last only so long as the tuberculin injections cause in a varying degree vascular changes and cellular infiltration about the tubercular areas, and cease as soon as the remedy is powerless to produce these. In the rabbit's eye this slight irritation can be maintained much longer than in lupus in man, and the result is correspondingly better and more permanent. How powerful a factor in antagonizing the progress of tuberculosis an artificially induced irritation of the surrounding tissues can be, is shown by the complete cures which often follow resection of tubercular joints, even though much of the infectious mass may unavoidably have been left in the joint. It has also been demonstrated clinically, and of late experimentally as well, that in tubercular peritonitis the traumatism of a laparotomy and the exposure of the serous membrane to the air are capable of producing in it a reactive irritation which enables the tissues to smother the onward progress of the more chronic bacillary infection, and apparently cures the disease.

In weighing the evidence offered by this study of the effect of tuberculin on the initial tubercular lesion as it occurs in the rabbit's eye, it should be noted that the eyes of the control animals are all destroyed often many months before relapses begin to occur in the treated ones, and that the relapsed lesions run a very chronic course. This treatment may be said, therefore, to produce a marked and undoubted curative influence upon the disease, but an influence which, though inhibitive in its action for long periods of time, rarely leads to a permanent cure in the initial lesion. I have not had an opportunity to study the effect upon these relapsed eyes of a renewal of the treatment.

The results of preventive inoculation are much more satisfactory and apparently more enduring. The rabbits which have survived the subcutaneous inoculation of living cultures of the avian tubercle bacillus of gradually increasing virulence and in graded doses,

have undoubtedly acquired a certain degree of immunity against subsequent eye inoculation with the mammalian cultures, which in some animals under my observation has persisted for over a year without the slightest evidence of a relapse. These eyes appear almost normal, little or no evidence of the virulent inoculation remaining save the corneal scar and slight adhesions of the pupil to the lens. Unfortunately here, as in the case of animals treated with tuberculin, apparent relapses occur, though here a study of the changes in the eye does not point so much to a true relapse as to imperfect and only relative protection, the disease from the first merely running a very chronic course. These cases are, however, by no means the rule, and the degree of immunity obtained appears in many instances of long duration. To test the permanence of the apparent immunity, reinoculation was practised after six months in the sound eyes of several of the animals. The changes in the eye produced by this followed to some extent the same typical course as in the first instance, and the disease ran a very chronic course, and in one instance aborted entirely, the second eye being restored as the first had been. This striking result is shown in the photographs of animal A, in which both eyes, six months and a year after the virulent inoculations, remain apparently normal. This was, however, the only animal in which so good a result was obtained. The other photographs were made from the same rabbits shown here last year, and were taken one year after the test inoculation. They illustrate admirably the degree and uncertainty of the protection realized, which, as is seen, may be either complete, partial, or entirely lacking.

As I pointed out, the reaction produced in the surrounding tissues by the introduction of the mammalian bacillus in the eye differs greatly in the prepared animals from that observed in the controls. In the controls the slight degree of irritation caused by the traumatism having passed away, but little is to be noted in the eye for ten days or two weeks, when the evidence of a gradually progressive tubercular process appears and goes on uninterruptedly to more or less complete destruction of all the structures of the eye. In the prepared animals, on the other hand, the introduction of the infectious material in the eye gives rise almost at once to signs of violent and at first steadily increasing inflammatory reaction, which,

however, in two or three weeks slowly begins to subside and may finally entirely disappear. The more marked and more immediate is this inflammatory reaction, the better the prospects that the tubercular process will be ultimately aborted, and that almost complete restoration of the eye will ensue in the animal under observation. Indeed, a very fair estimate of the degree of protection produced may be made, according to the early appearance and intensity of this primary reaction. Even in cases where it is slight, the tuberculosis runs a more chronic course than that observed in control animals, but nevertheless may ultimately end in complete destruction of the eye. It is evident that a profound impression of some kind has been made upon the defensive resources of the animals by the preventive treatment, for the manner in which they react to the test inoculations has been manifestly altered. This is in accordance with the observations of Kitasato, who, having succeeded in curing five guinea-pigs out of twenty-five treated by injections of tuberculin, found that cutaneous reinoculation was at once followed by intense local irritation, ending in the separation of a slough which left behind it a healthy granulating surface, no systemic infection of the animals resulting.

The introduction of living bacilli would appear necessary to the production of this relative immunity, and the inoculation of merely chemical substances contained in the cultures is powerless to produce it, for all attempts which I have made to protect rabbits with sterilized growths of the avian bacillus, whether killed by heat, light, time, or carbolic acid, have all proved negative. Curiously, however, in animals which have been prepared with dead cultures, the peculiar early reaction of the tissues to the virulent inoculation occurs to a certain extent; but the process goes on uninterruptedly to caseation and destruction of all the structures involved. The principle upon which the relative immunity thus obtained rests seems analogous to that which has governed Pasteur in his antirabic inoculations; *i. e.* the gradual habituation of the organism to a virus of greater virulence than that with which the test inoculation is to be made. In accordance with this view it may be noted that the occurrence of a tubercular process which has become arrested does not protect against another and frequently rapidly fatal invasion of the disease, and all attempts at protective treatment with

attenuated cultures of less virulence for the animal than those used in the test inoculations have, as far as I am aware, and many times in my own experience, proved entirely unsuccessful. We find, also, that while the rabbit, who is very much more susceptible to the avian than to the mammalian bacillus, may acquire a certain degree of immunity against the latter by preventive inoculations of the former, the guinea-pig, who can rarely and with great difficulty be killed by the avian microbe, even when enormous doses of these cultures are injected, is in no way protected by this treatment, a fact which I have several times proved experimentally myself.

All attempts at the production of artificial immunity to tuberculosis in animals have hitherto resulted in an unbroken record of failures, but recently Grancher and Martin claim to have succeeded in protecting rabbits, and Richet and Héricourt dogs, by preventive inoculations of avian bacilli. Their results show the same danger to the animals' health and life from the preventive treatment, the same uncertainty as to the production of immunity and the degree of protection which it affords as noted in my own experiments on the rabbit's eye. Richet and Héricourt have yet given no evidence as to the duration of the immunity they claim to have produced in dogs. Grancher and Martin's rabbits, however, outlived the controls by many months and even years, but in most cases ultimately succumbed to some complicating organic lesion other than tuberculosis, which is thought to have been the result of the toxic products injected in making the preventive inoculations.

Faint and fragmentary, therefore, as is the evidence that artificial immunity against tuberculosis is as yet anything more than a dream, this preliminary study of the effect of preventive inoculation upon the primary lesion in the rabbit's eye, when taken in connection with the experiments of the above-named observers, indicate a possibility of producing at least a relative degree of artificial immunity in this disease, and warrant the following conclusions :

1. Preventive inoculations of living cultures of avian tubercle bacilli cannot be made in rabbits without some danger to the animal's health and life.

2. The tubercular process induced in the eyes of rabbits which have been subjected to the preventive inoculations differs in its

course from that observed in the controls, and may even entirely abort, ending in an almost complete restoration of the infected eyes, a result never observed in the controls.

3. Uncertain, imperfect, and generally only relative as this artificial immunity against tuberculosis appears, it is nevertheless sufficiently marked to be demonstrable.

THE EFFECTS OF VARIOUS METALS ON THE GROWTH OF CERTAIN BACTERIA.

By MEADE BOLTON, M.D.,
ASSOCIATE IN BACTERIOLOGY, JOHNS HOPKINS UNIVERSITY.

(*From the Pathological Laboratory Johns Hopkins University.*)

NÄGELI[1] found that certain metals, even in minute traces, inhibit the growth of certain diatoms. Copper he found to be specially active. Pure gold he found to be inactive; but gold coins placed in water of a neutral reaction inhibited the growth of the diatoms. Certain bodies, such as sulphur, carbon, and the like were found to deprive the metals of their inhibitory power. If these substances were placed along with the metals in the water containing the diatoms, the latter were unaffected by the metals.

Miller,[2] of Berlin, tested the effect of various metals used in dentistry upon the growth of bacteria. Miller's method consists in inoculating a tube of melted jelly with a large number of organisms and pouring the contents of the tube out on a sterilized glass plate. Bits of the metal to be tested are laid on the jelly while this is still soft. Where the metals have an inhibitory effect upon the growth of the micro-organisms there is a clear zone left around the metal after the colonies grow out on the other parts of the plate.

The various commercial preparations of gold tested in this way gave the following results:

1. Velvet gold has no antiseptic properties.
2. Wolrab's have cylinders very little.

[1] Nägeli, C. von: Ueber oligodynamische Erscheinungen in lebenden Zellen. Denkschrift d. schweiz. naturforsch. Gesell., 1893, Zürich, Bd. xxxiii., 1. See also review in Botan. Centralbl., Bd. lv. 93.

[2] Miller: Demonstration einer Methode zur Bestimm. d. antisep. Eigenshaften v. Zahnfüllungsmitteln. Verhand. d. deutsch. odontolog. Gesell., 1889, Bd. i., 1, p. 34.

3. Pack's pellets inhibited the growth for about 5 mm. all round.

4. Quarter Century gold foil and Abbey's non-cohesive foil about the same as Pack's pellets.

5. Rolled gold and sponge gold had no effect.

6. Tin gold had much less effect than gold alone.

7. Tin and platinum had no effect.

8. All gold loses its antiseptic power on being glowed.

Behring[1] tested in the same manner the action of several metals upon the growth of the anthrax bacillus, diphtheria bacillus, bacillus pyocyaneus, cholera bacillus, glanders bacillus, and typhoid bacillus, with the following results :

Abbey's cylinders (gold) gave a clear zone of inhibition with anthrax bacilli (1.5 cm.), with diphtheria bacilli (3 to 5 cm.), with cholera bacilli (0.4 cm.), with bacillus pyocyaneus 1 cm.; but had no effect upon typhoid bacilli or glanders bacilli.

Silver leaf and metallic mercury, and to a small extent, copper, nickel, and zinc gave inhibitory zones. Tin, lead, and iron were negative.

Behring also tested certain insoluble salts of mercury, zinc, and lead. Calomel gave about the same results as metallic mercury ; the oxide of mercury was somewhat more active. Cinnabar was entirely indifferent. Mercury and its compounds had just the same effect on all the organisms examined. Gold, silver, and copper coins, and to a limited extent, nickel coin, had some effect. Gold coin had no effect on the typhoid or on glanders bacilli. The clear zones tested by inoculation into bouillon showed the microorganisms to be absent. Behring removed the metal and reinoculated the clear zones. In these reinoculations the growth was much retarded, showing that some of the metal must have been in solution in the medium. Behring observed a peculiar discoloration of the silver and lead with the typhoid and cholera bacilli, whereas, with the anthrax bacilli and the Finkler-Prior's and Deneke's spirilla there was no discoloration. Gold acts more powerfully upon the anthrax and pyocyaneus bacilli than silver does. Behring draws the conclusion that the metals are dissolved by the

[1] Zeitschr. f. Hyg., etc., 1890, Bd. ix., p. 482.

products of some of the bacteria more readily than by the products of others.

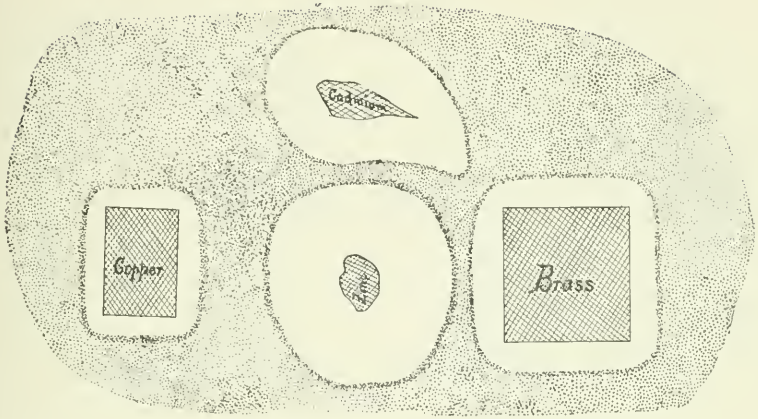
Uffelmann[1] tested the effect of metals on cholera bacilli by smearing the surface of coins with liquefied jelly cultures of cholera bacilli. The bacilli were dead in 17 minutes after they were smeared on a copper coin. Cholera bacilli in a cholera stool smeared on silver coins in the same way were dead in 25 minutes after they were put on. On a brass coin the cholera bacilli, in a liquefied culture, were alive after 30 hours, but dead after 60 hours On platinum foil there were living cholera bacilli after one hour, but not after 5 hours.

In the experiments given below I have made use of Miller's method already described. For the most part agar plates were used, and the metals were put on as soon as the plates were made. In some cases the metals were absolutely pure, in some cases they were commercial, but marked chemically pure, in one set brass foil was used, and a few preliminary experiments were made with impure metals. I am indebted to Prof. Morse of the chemical laboratory of the Johns Hopkins University, for absolutely pure zinc and cadmium. Prof. Chittenden, of Yale, kindly sent me a sample of pure silicon. The copper, silver, and gold I purified myself, with valuable aid from Dr. G. de Chalmot and Dr. H. M. Parks, both skilful chemists, formerly connected with the chemical laboratory of the Johns Hopkins University. The foils mentioned in the description of the experiments were kindly furnished me by Prof. Halsted, who used them in his experiments on the dressing of wounds. For the other metals besides those referred to I am indebted to Dr. Berkely, Pathological Laboratory, J. H. U.

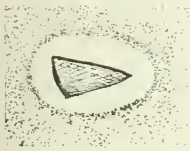
There was no special selection of cultures. These were taken of various ages, and were usually oblique agar cultures. In order to get the reactions described below it is necessary to inoculate the melted medium with a very large amount of the culture, four or five loops to a tube; where smaller amounts were used it was often impossible to make out anything but a clear zone, and the peculiar figures described below were not obtained. If the layer of the medium is too thick the reaction is also interfered with.

[1] Uffelmann: Beiträge zur Biologie des Cholerabacillus. Berlin. klin. Wochenschr., 1892, No. 48, p. 1212.

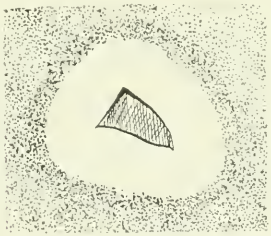
PLATE I.



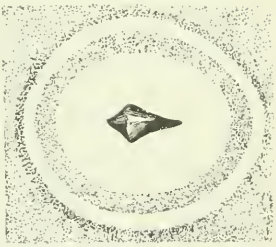
1 Staphylococcus pyogenes aureus.



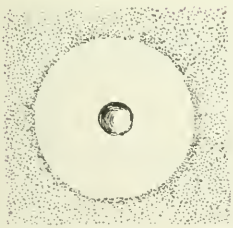
2. Staphylococcus pyogenes aureus. Cadmium.



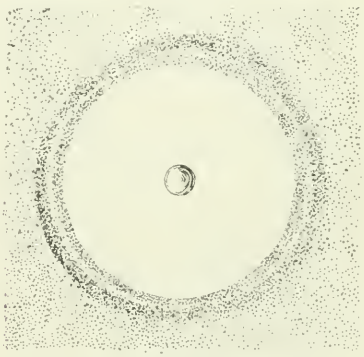
3. Bacillus typhi abdominalis Cadmium.



4. Bacillus anthracis. Cadmium.



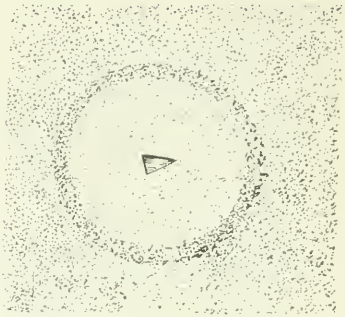
5. B. Coli communis. Mercury.



6. Bacillus typhi abdominalis. Mercury.

PLATE II.

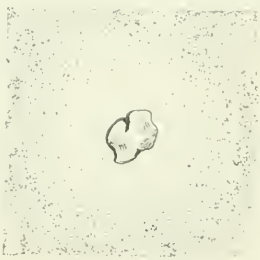
7. Staphylococcus pyogenes aureus. Antimony.



8. Bacillus coli communis. Antimony.

9. Bacillus anthracis. Antimony.

10. Bacillus typhi abdominalis. Antimony.



11. Cholera. Antimony.

Experiments with Copper.

A few preliminary tests were made with various micro-organisms with ordinary copper wire and with copper coins. The wire and coins were merely polished with ammonia and sand and rinsed with water. The rest of the experiments were made with pure copper and with copper foil.

There is no marked difference in the behavior of the micro-organisms toward the copper in these different forms. In all cases there is a clear zone, in some cases narrower, in others wider, and then a narrow zone where there is increased growth. This intensified zone does not have as sharply marked borders as with certain other metals. Both the clear zone and the intensified zone vary appreciably in width, even with the same micro-organism. With staphylococcus pyogenes aureus (Plate I., Fig. 1) the clear zone measures in some cases as much as 5 mm. in width, and in some cases only 2 mm. The average width of the clear zones in fifteen of the experiments with copper foil is 3.1 mm. With the micro-organisms of anthrax, cholera, typhoid, and the colon bacillus the clear zone varies from 1 mm. to 5 mm. in width with the same organisms at different times. In nearly all cases the medium around the copper becomes greenish and the foil becomes dissolved away, sometimes entirely disappearing.

Experiments with Brass.

The tests with brass were made exclusively with brass foil. The zones obtained with the different micro-organisms were similar to those obtained with copper. The organisms tested with this alloy were staph. pyog. aureus (Plate I., Fig. 1), typhoid bacillus, b. coli communis, b. anthracis, b. choleræ Asiat., b. prodigiosus, b. pyocyaneus. The average width of the clear zones in fifteen of the experiments with staphylococcus pyog. aureus is 2.5 mm.

Experiments with Silver.

The results with silver were somewhat less uniform than with copper and brass. A number of preliminary tests were made with polished silver coins, but no record of these was kept. There

seemed, however, to be no striking difference between the results with the coins and the results subsequently obtained with carefully purified silver.

The zones obtained around the silver with staphylococcus pyogenes aureus are first a clear zone, 1 to 2 mm., sometimes even less than 1 mm., followed by a very narrow intensified zone; the intensified zone is sharply marked off from the clear zone and not so sharply marked off on the outside. The intensified zone is better marked with silver than with copper or brass, but it is also narrower. With anthrax cultures the action of the silver varied considerably in different cases. In some cases no zone at all was observable, in some cases there was a zone of about 7 mm. where the colonies were not as thick as on the rest of the plate, and in still others there was a perfectly clear zone of about 1 mm., followed by a zone of 5 or 6 mm. where the colonies were not as thick as on the rest of the plate. With cholera bacilli there was a clear zone, 5 mm. broad, followed by an indistinct intensified zone. With typhoid bacilli there was a clear zone about 1 mm., the intensified zone was faint. With the colon and b. pyocyaneus there was a clear zone about 5 mm. wide, then an intensified zone quite sharply marked toward the metal, but shading off gradually on the outside.

Experiments with Gold.

The effect of gold was tested in a few cases with gold foil, and a great many experiments were made with purified gold. No inhibition was observed with staph. pyog. aureus, colon bacillus, typhoid bacillus, or cholera bacillus. In some cases there was inhibition of the growths of anthrax cultures, and this difference of action is probably to be accounted for by the fact pointed out by Miller, that gold when freshly glowed has no inhibitory power. In those cases where inhibition was noticed the gold had not been glowed for several weeks. The clear zones when obtained were sharply marked and about 1 mm. broad, and there was also some intensification outside.

Experiments with Magnesium.

The magnesium used was the ordinary magnesium ribbon. Tests were made only on staph. pyog. aureus and the cholera bacillus.

With both of these organisms there was a clear inhibitory zone, followed by a zone of increased growth, sharply marked off from the clear zone and gradually fading out on the outside. With the staphylococcus aureus the clear zones average about 1 mm., with cholera bacillus the clear zones average about 2 mm. In every case the bit of metal was raised up above the medium by an accumulation of gas bubbles.

Experiments with Zinc.

A good many experiments were made with ordinary scrap zinc, cast in a sheet, but no note was kept of these. There was a clear zone, however, in every case, and there was probably not much difference between the action of this and of the pure zinc.

With pure zinc all the organisms tested give a broader or narrower clear zone, surrounded by an intensified zone. There is also always a milky discoloration of the medium all around the metal, showing that the metal has been acted upon. This discoloration disappears on the addition of an acid or an alkali.

With staphylococcus pyog. aureus (Plate I., Fig. 1) the clear zone measures from 5 to 8 mm. in breadth, the average being 7 mm. The intensified zone is very evident, but not sharply marked enough to measure. With cholera there is a wide, clear zone, about 1.5 cm., and the effect of the metal is seen as far as 3 cm. away from the metal. With other organisms the clear zone is usually 5 mm. or more broad, followed by a broad intensified zone that is not sharply marked.

Experiments with Cadmium.

All experiments with cadmium were made with the pure metal. With this metal the reactions obtained with various micro-organisms differ quite strikingly, as a rule. With staphylococcus pyogenes aureus (Plate I., Fig. 2) there is a clear zone from 5 to 9 mm. wide, varying in different plates, but no markedly intensified zone. With the colon bacillus the clear zone is about 4 mm. wide, surrounded by a very much intensified zone of 4 mm. With typhoid bacillus (Plate I., Fig. 3) there is a clear zone, 5 mm., then a faintly intensified zone 2 mm. broad.

With the cholera bacillus there is a clear zone from 5 to 9 mm., not sharply marked on the outside. The most peculiar zone of any with any micro-organism is that obtained with the micro-organism of anthrax and the metal cadmium. In this case (Plate I., Fig. 4) there is a perfectly clear zone, 5 mm. wide, then an intensified zone of 2 mm. breadth and a second inhibitory zone 1 mm. wide. In some cases this second inhibitory zone is not entirely free from colonies, but it can always be made out very distinctly.

Experiments with Mercury.

There is considerable difference in the behavior of different micro-organisms toward mercury. The zones obtained with staphylococcus pyogenes aureus are first a clear zone about 7 mm. around the metal, followed by a slightly intensified zone which varies in different cases from 1 to 3 mm. in width. With the cholera bacillus there is a clear zone 2 mm. around the metal, then a very narrow intensified zone that is well marked. With bacillus pyocyaneus there is a clear zone 4 mm. broad around the metal and outside an intensified one, sharply marked toward the clear zone and shading off gradually on the outside. With the micro-organism of anthrax there is a broad, clear zone, 9 mm. around the metal, surrounded by a very slightly intensified zone that is not sharply marked. The colon bacillus obtained from normal feces of different individuals and the typhoid bacillus also obtained from different cases show each a characteristic behavior toward the mercury. With the colon bacillus (Plate I., Fig. 5) there is a clear zone often 7 mm. broad, sharply marked on the outside, then an intensified zone gradually shading off on the outside. With the typhoid bacillus (Plate I., Fig. 6) the clear zone is much broader, often 1 cm. across, but the peculiarity is the character of the intensified zone. This is about 2 mm. across, more intense on the outside away from the metal, and in different cases is more or less double, *i. e.*, there is a narrow, almost clear zone running all around which divides the intensified zone into two zones. Although the number of experiments with both the colon bacillus and with the typhoid was not inconsiderable, it would hardly be safe to regard the reactions as characteristic until a greater number of tests have been made.

Experiments with Aluminium Foil, with Charcoal, Silicon, Niobium.

A number of tests with charcoal gave no reaction. Aluminium, silicon, and niobium also failed to show any reaction.

Experiments with Antimony.

Antimony with staphylococcus pyogenes aureus (Plate II., Fig. 7) gives a clear, sharp zone, about 1 cm., then a zone about 5 mm. wide where there is diminished growth. In one of the plates with aureus there was only a very narrow, clear zone. The reason for this difference was not apparent. With the colon bacillus (Plate II., Fig. 8) there is an inhibitory zone 8 mm., where the growth of colonies is somewhat thinner than on the rest of the plate, but no clear zone. The intensified zone is quite distinct and about 1 mm. broad. With the typhoid bacillus (Plate II., Fig. 10) there is an almost clear zone, 1 cm., then an intensified zone, 2 mm. broad. With the anthrax bacillus (Plate II., Fig. 9) there is a perfectly clear zone, 1.8 cm., then an indistinct, intensified zone. With the cholera bacillus (Plate II., Fig. 11) there is no sharply marked clear zone, but diminished growth can be made out as far as 1.5 to 2 cm. around the metal.

Experiments with Bismuth.

Staphylococcus pyogenes aureus with bismuth gives a clear zone about 2 mm. wide and an indistinct, narrow, intensified zone. With anthrax cultures there is a clear zone, 1 mm. Pyocyaneus, cholera, typhoid, and colon bacilli, gave no reaction with bismuth.

Experiments with Iron.

A bright polished wire nail gave a clear zone about 7 to 10 mm. with the typhoid bacillus and with the colon bacillus. There was also discoloration of the medium around the nail. Other organisms were not tested.

Experiments with Nickel.

Pure nickel failed to give any reaction with most of the micro-organisms tested. There was a clear zone with an anthrax culture in the only test that was made with this organism. A nickel five-cent coin gave a clear zone with typhoid bacilli and with colon, but it was possible to detect traces of copper in the medium around the coin.

Experiments with Platinum.

Platinum wire and platinum black failed to give any reaction with any of the micro-organisms tested.

From the above results it is evident that certain metals have at least no marked effect upon the growth of the bateria tested, and it is notable that it is precisely those metals that are resistant toward chemical reagents in general which fail to show any reaction or do so only to a limited extent. On the other hand, metals that are readily attacked by chemical reagents all exhibit a marked inhibitory action upon the growth of the bacteria. The effect is, therefore, probably due to a solution of the metal in the medium, and putting bits of metal on the cultures is really equivalent to the addition of a small amount of that salt of the metal formed by the action of the nutrient medium. Traces of the metal may moreover be detected by chemical reagents in the nutrient medium surrounding the metal. This was done in many cases by simply adding the chemical reagent in small drops to the medium. In some cases the medium was cut out, incinerated on platinum foil, and tested by Behrens' methods.[1] But in many cases a chemical test was not necessary, for the discoloration of the medium alone sufficed to show that the metal had gone into solution and with the copper and brass foils there were visible holes dissolved out of the metal. Behring states that the solution of the metal is more or less affected by the products of the growth of the different bacteria. However this may be, some metals are dissolved out in sterile media and may be detected by chemical means.

[1] Behrens: Beiträge zur mikro-chemischen analyse. Zeitsch. f. an. Chem., Jahr. 30, Wiesbaden, 1891. [Detailed in full in Ann. de l'Ecole polyt. de Delft, 1891.]

The explanation of the clear zones is thus quite evident, but the explanation of the intensified zones and of the second inhibitory zone, sometimes seen, is not very apparent. The ideas suggested themselves that the bacteria are driven off from the neighborhood of the metal and collected in the intensified zone, or that the presence of a very small amount of the metal in the medium attracts micro-organisms from all sides. Neither of these explanations seems probable in a solid medium, particularly as many of the organisms tested have no independent motion, and, moreover, the results of experiments made to test this point were negative. These experiments were made as follows: Petri dish cultures of various bacteria, particularly of the motile organisms, were made in very dilute agar, so that the organisms could move about freely and at the same time not be much affected by jarring. After these cultures had grown out, bits of metal were put on the plates and then studied with the microscope. Drop cultures made with diluted agar and having a very small bit of metal on them were also tried. The organisms did not seem to move in any one direction more than in any other.

Another explanation, however, seems to me to explain satisfactorily the clear zone immediately around the metals and the intensified zone, namely, that the dissolved oxides or salts of the metals are in too great concentration in the clear zone, and the trace that is present in the intensified zone may stimulate growth. This does not explain the second inhibited zone.

The length of time it is necessary to leave the metals in contact with the agar, in order to develop inhibitory action, was tried with brass, copper, cadmium, and zinc. Plates of staphylococcus pyogenes aureus were made in the usual way and the metals put on and removed at various intervals. With cadmium there was a clear space where the metal had lain and for 1 mm. around where the metal had been left on for a minute. Where the metal had been left on for three or four minutes or more, the clear space usually extends over 3 mm. around where the metal has lain. With zinc the results are similar as regard length of time, but the edges of the clear zone are not well defined and there is an intensified zone that is not apparent with cadmium. With brass there was no effect produced by leaving the metal on for 36 minutes; after this there was more

and more marked inhibition up to 50 minutes, but no clear space except where the metal was left on for a longer time than this. With copper no visible effect was produced in less than 36 minutes. After this time there was more and more marked inhibition, but only where the metal had been allowed to lie on for 50 minutes was there a clear space.

Just how far the reactions described above are constant and characteristic will have to be determined by future experiment. It seems probable that they would be constant under the same conditions, since the number of experiments is quite large and the results were gratifyingly uniform, especially in those cases where the figures produced are peculiarly striking. These particularly were repeated a great many times.

DISCUSSION.

Dr. W. H. Welch: I am familiar with these investigations, and I have nothing to add to what Dr. Bolton has said. The most mysterious thing is the clear zone outside of the intensified zone. There is no difficulty in understanding the presence of the first clear zone immediately around the metal. This is unmistakably due to a solution of the metal in the form of oxide or salt. The most probable explanation of the intensified zone is that there is a minimal amount of the metal there which is favorable to the growth of the bacteria, whereas the larger amount in the clear zone is a poison to bacteria and prevents their growth. This fits in with many biological and therapeutic facts.

Dr. Theobald Smith: I would like to ask Dr. Bolton whether he paid any special attention to the culture medium used; whether, for instance, he used meat extract of the same quality for all of these experiments, or whether he used beef purchased in the market from time to time.

Dr. Bolton: I used beef extract of the same quality all the time.

Dr. Theobald Smith: The beef which we buy varies so much, especially in the amount of sugar (dextrose) it contains, that the bacterial products vary very much in different batches of culture media. At one time we may get no acid reaction from an organism, and at another we may get a strongly acid reaction from the same organism, owing to absence or presence of dextrose in the meat used. It would be of interest to know how the figures described by Dr. Bolton would vary when variable quantities of sugar are added to the culture medium.

SOME OF THE CHEMICAL AND BACTERIOLOGICAL CHARACTERISTICS OF MILK.

By T. M. ROTCH, M.D.,
OF BOSTON, MASS.

THERE are certain questions regarding the chemistry of milk which, though not necessarily of vital importance to its use as a food, are still sufficiently so to make them worthy of our investigation. The first of these questions which I shall consider is the reaction of cow's milk both at the time when the cow is milked and later in its use for food preparations. This question of reaction is of so much greater importance in connection with the feeding of infants during their first year than for the later periods of life, that I shall discuss it with special reference to infant feeding. The importance of the subject lies in the well-recognized fact that the infant's digestive functions have been from time immemorial best adapted to the digestion of an alkaline or neutral fluid rather than to an acid one. Human milk has proved to be the food on which the greatest number of infants live and thrive during the first year of their lives, and on which the smallest number die proportionately to any other known food. Whether the moderately alkaline reaction of human milk is an important factor in the problem of infant feeding is a question which future investigation alone can completely prove, but with our present knowledge we are not yet prepared to dispense with even the least important of the many factors which make up this problem. At any rate we should be very suspicious of a breast milk which showed an acid reaction. In the preparation of food from cow's milk, according to the latest experiments by means of modification, the best results have been obtained from making the reaction of this food correspond to that of normal human milk. This, up to the present time, has best been done by means of the addition of

an alkali, which is the only foreign element which it has been found necessary to employ.

My attention was first drawn to the possibility of obtaining an alkaline cow's milk corresponding in its reaction to that of human milk by Mr. G. E. Gordon, who has, by his extended and intelligent investigation of this subject carried on for so many years in the West, given such a stimulus to these questions of chemical interest. Many years ago it was noticed that cows fed on certain pastures such as occurred in Kentucky, represented by the Kentucky blue grass, and also in many other parts of the West, produced at the height of the season of such grass a product which was alkaline rather than acid, and which remained alkaline for a number of hours after milking. It is also, of course, well known that milk in general, wherever it is produced throughout the world, has an acid or at least an amphoteric reaction. This information at once incited the investigation of the food values which existed in these peculiar pastures. Careful analyses showed that the nitrogenous elements of this grass had a certain proportion to its carbohydrates, namely, about 1 to $5\frac{1}{3}$ (Kuhn). It has also been noticed by this same class of observers, from whom we have derived the only real knowledge which we have of this subject, that cows which are fed in their stalls on comparatively dry foods produce a milk which is distinctly acid in its reaction. We would naturally suppose that by merely combining nitrogenous and carbohydrate foods in the proportion of 1 to $5\frac{1}{3}$ the resulting product would resemble closely the product of the cows fed upon the pasture grasses already mentioned. This, to some extent, has proved to be true, but not so completely as is to be desired for the precision needed in infant feeding. It is therefore of the greatest importance to the solution of this question that experiments made in supplying the carbohydrate proportion of the food by feeding freely (ten pounds to each cow daily) with sugar beets of the highest saccharinity has accomplished empirically unlooked for results.

The cows which were experimented with in obtaining these results were under observation for three months, and were cared for in the same barn and under the same general conditions. Two-thirds of this herd were fed on the ordinary food ratio of 1 nitrogenous to $5\frac{1}{3}$ carbohydrates. The remaining third of the herd was

also fed on the same food ratio, but this ratio, so far as the carbohydrates were concerned, was made up partly by Austrian sugar beets grown for this purpose. No beets were given to the first two-thirds of the herd just spoken of. During these three months when the experiments were being made the reaction of common litmus paper was constantly as follows: the cows fed partially on the beets showed neutral or feebly alkaline reaction, and the cows that received no beets showed a uniformly acid reaction.

A still more delicate test of the reaction of the milk of the entire herd was made by Dr. Austin Peters, of Boston. Hay and grain, as previously stated, were given without beets to two-thirds of the herd, and ten pounds of beets for each cow continued to be fed to the remaining third. The milk of the whole herd was then mixed together in one vat, was tested in the vat, was then quickly transported to the laboratory, a distance of twelve miles, and again tested. The results of these experiments were as follows. The milk from the cows which had been fed with beets was tested directly in the pails at a temperature of 93° F.

Blue litmus paper gave no change whatever.

Red litmus paper was turned slightly blue.

Cochineal and ammonia paper turned still bluer.

The next experiment was made directly from the vat, which, as I have already stated, contained the mixed milk of the whole herd. The temperature was 42° F.

Blue litmus paper showed no change.

Red litmus paper was turned slightly blue.

Cochineal and ammonia paper was turned still bluer.

The same milk was then carried twelve miles, and on being examined in the laboratory with cochineal and ammonia paper turned the paper just as blue as when the milk was tested at the farm. This second experiment is of great interest as showing that the product of the cow can not only be made to correspond to that of human beings, by means of perfectly natural feeding and under perfectly normal conditions, but that this alkaline modification can be produced to such a degree that one-third of the milk is sufficient to destroy by its alkalinity the acidity of the remaining two-thirds.

The next experiment is a question of bacteriology, and is also

of considerable importance in the practical use of cow's milk as a food. It has already been found by certain observers that the first portions of milk drawn from the human breast may contain bacteria, while the later part of the milk is sterile. Acting on Mr. Gordon's suggestion, Dr. Austin Peters made the following experiments at the Walker-Gordon barns to determine whether like conditions existed in the milking of cows. Dr. Peters was dressed in a freshly boiled white suit and cap, and had his hands and arms thoroughly washed with a 1 : 1000 bichloride of mercury solution. The cow's udder, teats, flanks, sides, groins, and abdomen were also washed with the same solution and dried with a freshly boiled cloth. The milking was then done by Dr. Peters into sterile bottles with the following results :

Of the four cows milked for this experiment, selected without special reference, the bottle No. 1 in each of the following tables represents the first portion of the milk drawn by the hand of the milker directly into the sterile bottles. No. 2 in each table represents milk drawn through a sterile canula directly into the bottle, while Nos. 3 and 4 respectively in each table represent milk drawn by hand after more than one-half of the udder had been emptied. A bacteriological examination of the milk in these bottles by Dr. A. K. Stone gave the following results :

Bottle.	Colonies.	Colonies.	Colonies.	Colonies.
1 . . .	141	157	19	53
2 . . .	0	0	1	2
3 . . .	0	6	0	0
4 . . .	0	0	1	2

To summarize the above, we find that the direct milking of the first half performed by sterile hand shows a milk with a comparatively large number of micrococci and fine bacilli of the same general appearance respectively. We find further, that the milk drawn through the sterile canula was practically sterile, and the milk drawn in the second half of the milking by hand was so uniformly sterile as to awaken the suspicion that the isolated colonies might have been the result of the manipulation between the "cow and the plate."

These experiments at once provide us with a means of pro-

curing a milk practically sterile but not sterilized. This experiment also seems to prove that the bacteria which are found in cow's milk do not necessarily come from external sources, whether they be of the cow herself or her surroundings, but that they may also come from some part of the milk tract between the udder and the end of the teat. These conclusions, it may be said, are made with reference to healthy cows.

Analysis of the Mineral Matter of Human Milk.

Up to the present time, although a certain number of analyses of the mineral matter of human milk have been made, yet the results for various reasons have been deemed unsatisfactory. Such large quantities of milk are needed for a satisfactory determination of the percentages of each element which make up the total amount, that this in itself has been an important reason for failure in accuracy. The mineral matter of cow's milk on the contrary has not met with the same difficulty in its determination, and has been presented to us in its elemental percentages in a reliable form. As it has always been known that a radical difference exists between these elemental percentages in cow's and in woman's milk, the knowledge of the exact percentages which exist in the latter has lately become of still greater importance, since such decided advances have been made in the modification of the other elements of cow's milk.

With the view of making some advance in this difficult question and providing for the milk modifiers of the future a more exact basis for perfecting a substitute food resembling as closely as possible the product of the human breast, I undertook, in the spring of 1893, to procure an unusual and sufficient quantity of human milk for analytical purposes. In the course of a few weeks, by means of the concerted action of numerous assistants, notably that of Dr. Stickney, I collected five and a half litres, which is an unusually large quantity for experimental purposes. This milk was immediately reduced to its mineral constituents in the laboratory of Dr. Charles Harrington. The analysis of this large amount of mineral matter was then jointly made by Dr. Charles Harrington and Dr. L. T. Kinnicutt, with the following result:

Unconsumed carbon		0.71
Calcium phosphate	$Ca_3P_2O_8$	23.43
Calcium silicate	$CaSiO_3$	1.35
Calcium oxide	CaO	2.54
Magnesium oxide	MgO	0.96
Iron oxide	Fe_2O_3	0.40
Alumina	Al_2O_3	

I make no report on the potassium and sodium salts, as their analysis was not considered satisfactory, and is being made over again.

In comparing the previous analyses which have been published, and which can be found in Konig's *Nahrungsmittel*, II., 2. Auflage, with this new analysis we must remember that the previous analyses were made some years ago. In the last few years the processes which are employed have been so much more exact that the results must be considered far more trustworthy than those made at an earlier date. It is not remarkable, therefore, that decided differences should be found between this new analysis and those which have hitherto been made, and presumably this last analysis is the correct one. It has been made with the most absolute care, and by means of the most improved technique, by two eminently competent and well-known chemists, who in their work have acted as controls on each other. In this way great precision has been attained.

The chief differences between this new analysis and all previous ones are as follows:

1. The phosphoric acid is less than half as much as previously reported.

2. The magnesia is also less than half as much.

3. Silica and alumina are present; they have not been returned in any previous analysis.

Assuming the truth of the statement that the constituents of the mineral elements of human milk are subject to great fluctuation according to individuality and other causes inherent to the human race, it is right to presume that the mineral matter examined by Kinnicutt and Harrington, being the product of a large number of women, is a fair average specimen.

DISCUSSION.

Dr. F. Forchheimer: In cities the great majority of specimens of milk has an acid reaction. The normal reaction of milk is alkaline, rarely amphoteric, so that the acid reaction alone implies something abnormal in the milk. The work of Dr. Rotch heretofore has been in the direction of supplying good milk for infant feeding, but, it seems to me, he has now hit upon the fundamental principle, and we may hope to find out what is implied by normal milk if these investigations are continued. It has seemed to me futile to add alkalies to acid milk, as we are simply adding another element to milk that is already bad.

A great number of troubles in infants arise from impure milk, and just as the surgeon protects his patients from sepsis, so it is the duty of the physician to protect infants from milk sepsis. There is more room for reform in this connection than almost any in which the physician has any dealings with, and it would be very well if each one of us in our limited circle would take this question in hand and act in the direction of reform in dairies. It is here that we must look for our pure milk—the attempts heretofore made to change impure milk must be futile and dangerous. Anyone who has worked with milk, as all of us have who have to do with the feeding of children, will recognize immediately the importance of this subject. Anyone who has taken the trouble to make the simplest sort of test with milk, to centrifugate and examine impurities, will come to the conclusion that the best samples of milk in cities are extremely impure and very dangerous. If anyone has ever seen a centrifugate of a large quantity of milk, say ten to fifteen gallons, he knows that it almost acts as inhibitory to the drinking of milk.

Dr. Theobald Smith: As bearing on the subject of bacteria in the milk ducts I may give one interesting illustration. Milk drawn into a sterile bottle with ordinarily clean hands was kept on ice for a few hours, and then plate cultures made therefrom. After development these showed a large number of colonies of *staphylococcus pyogenes aureus*. The guinea-pigs which were inoculated in the peritoneal cavity with some of this milk died in from one to three weeks with subperitoneal abscesses, suppurative pericarditis, and other lesions. This shows that milk may be directly infected from the udder with disease germs other than those of tuberculosis.

In reference to the centrifugalizing of milk, we have found that the deposits, so far as the morphological elements are concerned, are made up largely of polynuclear leucocytes. In some samples of milk these were exceptionally abundant. In one such sample tubercle bacilli were detected by the inoculation of guinea-pigs. I do not know that there is any direct relation between extensive leucocytosis in milk and tuberculosis of the

udder, but it might be well to bear the probability in mind in future investigations.

Dr. T. M. Rotch: I would draw your attention to the practical results obtained from the bacteriological examinations, namely, that where you cannot provide otherwise for sterile milk you can get it by using the last half of the milking. You can also, by regulating the feeding of the cows as I have indicated, prepare a food which, while closely simulating human breast-milk, need have no ingredient foreign to human milk added to it.

OSTEOMALACIA, WITH A NEW CASE.

By GEORGE DOCK, M.D.,
OF ANN ARBOR, MICH.

Mrs. R., aged twenty-four years, housewife, was admitted to the hospital of the University of Michigan, April 1, 1892, and gave the following history:

Father in good health, but appears to have had syphilis. Mother has a goitre, "large as a man's head," of twenty-five years' duration; otherwise well. Patient has four brothers, all strong and healthy. Neither the patient nor the father know of any bone disease or malignant disease in the family.

Patient was born in northwestern Pennsylvania, but has lived in the northern part of the lower peninsula of Michigan for thirteen years. As a child patient was not strong; was frequently affected with diarrhœa; had whooping-cough; in the fall of 1891 had a severe attack of diphtheria. Menstruation began at thirteen and was normal. At seventeen was married to a healthy young man who worked a small farm. Two years after marriage the first child was born. During the pregnancy there were frequent attacks of rheumatic pain which patient cannot clearly describe. Delivery was normal, but there was difficulty in the removal of the placenta. This was followed by hemorrhage so severe that patient "nearly bled to death." The hemorrhage was checked by cold douches which were followed by severe pain in the pelvis. This pain has continued, varying in severity to the present time. Notwithstanding the complications mentioned, the patient nursed the child (a boy) for fourteen months. Two years after the birth of the first child she had a second. The placenta was again adherent and its removal followed by hemorrhage. She nursed this child (girl) for fourteen months. The children, five and three years of age, are well grown and healthy. The boy has a congenital deformity of the right thumb, the metacarpus and first phalanx being absent and the terminal phalanx rudimentary.

In the spring of 1890 pains came on gradually in the knees. The joints were sore and painful, especially in bad weather, increased by walking, but there was no stiffness. There was also pain in the liver region and between

the shoulders. The pain was severe and constant, and gradually grew worse for about six months, when it remained about the same. On the 25th of December, 1890, the patient slipped while getting out of a sleigh, and fell lightly to the ground. On rising she found the left femur broken at the upper part. A physician could not be obtained for a day. There was great pain, but no swelling. The thigh was bandaged and extension applied with a twenty-pound weight. After eight or nine weeks the bone had united with slight deformity. The patient could not walk, however, but seemed to have lost all her strength. The pains in the legs and body continued, but the patient was able to sit up nearly every day. In the summer of 1891 the patient was treated in a homœopathic hospital, probably for ununited fracture, though perhaps for rheumatism. There was no improvement, but the condition grew worse. Painful cramps began in the right leg. At that time the patient noticed that her right leg was "drawing up," and that her heart beat rapidly.

In August, 1891, while raising herself in a chair she strained the right arm. Since then arm and shoulder have been painful. In December, 1891, she went to bed on account of severe pain in the pelvis, worse at the menstrual period, and cramp in the legs, and has not been able to sit up since then. She has become very weak; has frequent "fainting spells," and palpitation of the heart. The appetite is very poor, vomiting after meals rather frequent. The bowels are regular. Sleep is interrupted by coughing and pain. Cough is frequent, with abundant expectoration. Menstruation absent for three months.

Status præsens, April 1, 1892. The patient lies on her back; her expression indicates great pain. There is slight deafness and the memory and intelligence of the patient are very poor. The normal height is not known: the patient measures now 139 cm. from vertex to right heel. Weight has been 148 pounds, now not more than 110. The bones of the upper part of the body and arms are slender; those of the legs thick. The skin and mucous membranes are pale. The panniculus is wasted everywhere; the muscles small and flabby. Tongue yellow coated, voice nasal. Thyroid enlarged, especially the middle and right lobes. This has existed since puberty.

Thorax narrow, flattened in front and at the sides. The manubrium concave, especially on the right side. The ribs are very yielding and elastic, painful on pressure. On the right side in the habitual position, the ribs are in contact with the crest of the ilium; on the left side the twelfth rib is a hand's breadth from the ilium. The distance between the anterior superior spines is 23 cm, between the iliac crests 28.5 cm. The iliac bones yield when pressed together and spring back when released. The pelvis is very flat, the promontory being on the same plane as the pubis. The promontory could not be reached when examined *per vaginam*. (The pelvis was examined in the obstetric clinic, but the notes of measurements have been lost.)

The left femur lies in front of the right, resting on the latter just above the knee. The bone is strongly curved forward and then inward, at the upper third, where there is a fracture with great thickening of the bone. The lower end of the left patella is 28 cm. below the pubis. The femur cannot be adducted or abducted on account of spasms in the muscles. The shaft of the femur is thickened in its whole length. There is free motion in the left knee. The left tibia is well formed, as is also the foot and ankle.

The right femur, greatly thickened, is curved outward in the upper part; inward below. There are fractures at the upper and lower thirds, and just above the condyles. There is also crepitus at the upper end, apparently in the surgical neck. The knee is turned in and a little to the right of the median line. The lower end of the patella is 35 cm. below the edge of the pubis. There is crepitus in the knee-joint. The right tibia is thickened, especially at the lower third, where there is a large hard mass. The right foot and ankle are well formed. The heel extends 5 cm. beyond that of the left foot.

During the examination strong contractions came on in the muscles of the legs, especially those of the right thigh. These could be brought on by a slight touch, but were sometimes spontaneous. For this reason the knee reflexes could not be carefully examined. There is no ankle clonus on the left side, but it is present on the right.

The clavicles and arms show no deformities. Motion of the right arm is painful.

Examination of mouth, pharynx, and larynx negative. The copious, purulent sputum (pharyngeal) was examined many times for tubercle bacilli, with negative results.

Percussion and auscultation of the lungs negative.

Apex beat in the fourth intercostal space, just outside the nipple line. There is a strong impulse over the whole cardiac area. The absolute heart dulness begins on third rib and extends to the position of the apex beat and to the left edge of the sternum. The heart's action is very rapid, but regular. The first and second sounds very much alike at the apex. The pulmonary second sound is loudest just below the clavicle and ends in a distinct click.

Radial pulse 135, regular, small, tension low.

Examination of abdomen negative. Liver dulness from the fourth intercostal space in the right parasternal line to two fingerbreadths above the costal margin in the same line. In the median line the dulness ends just below the tip of the ensiform.

Splenic dulness not enlarged.

The urine was examined frequently during the patient's stay in the hospital; but as it was often passed involuntarily systematic quantitative examinations could not be made. Quantity: 900–1500 c.c. (twenty-four hours). Sp. gr.: 1008–1014. Reaction: usually alkaline. Color: pale yellow, turbid. Odor: peculiar, disagreeable, "onion" odor. Albumin:

always a trace, to about one-eighth bulk on standing. Albumose was usually present in small quantity; after precipitation of the albumin by acetic acid and heat and filtering, the filtrate gave positive tests, as precipitation with HNO_3 in the cold, disappearing on heating. Indican: always in slight excess. Diazo-reaction: usually a deep orange-red. At one time for three successive days, in connection with a rise of temperature of unknown origin, gastric disturbance, and headache, a reaction was obtained of deep garnet-red color, with pink foam. Fehling's test always negative. Urea: 14 to 21 grm. in twenty-four hours. Numerous tests for lactic acid negative. Sediment: always a heavy deposit of triple phosphate crystals, calcium oxalate, and amorphous phosphates; many leucocytes, epithelial cells, cylindroids, and occasionally a few short hyaline casts.

During the first month after leaving the hospital, urine was examined a number of times, showing absence of albumose, decrease of albumin. Urine usually acid, with small amount of sediment.

From September, 1892, until time of death, small calculi were constantly passed with the urine. These were either very hard, shining, sharp-pointed crystals of calcium oxalate, or dark-brown, smooth, and soft concretions of calcium phosphate. During this time the urine was alkaline. Sediment was so great that the pus-basin used as a urinal would be heavily coated. Masses of phosphate "mud" were frequently passed, consisting of thick deposit of "coffin-lid" and amorphous phosphates; albumin constantly present at this time, but not in large amount; albumose in small quantities.

As urine could not be collected with any accuracy, the exact quantitative estimation of phosphates could not be made.

For about six weeks the patient grew worse. The temperature rose daily to 102° or 103°; there was frequent vomiting of food and bile, several times mixed with blood. Patient could not move at all, and necessary moving caused intense pain and contractures. Spasmodic contractions, often spontaneous, were frequent, especially in the muscles of the thighs. Gradually the femurs were bent farther inward and upward, so that the legs were crossed above the knees, the left femur lying upon the right, as in the photograph. There were also cramps in the right arm.

From two to five times daily there were attacks beginning with dizziness and passing into unconsciousness. The pupils dilated; head moved from side to side; there was marked tremor of right extremities, beginning in fingers, involving the whole arm and then appearing in the leg. These attacks lasted from two to ten minutes, and were followed by intense headache.

About the middle of May improvement began. Vomiting ceased; appetite and bowels became normal; fever disappeared, and the patient had no more fainting-spells. The cramps and pains also decreased; and the softening and bending of the bones seemed to be at a standstill. By August 1st the condition had become very much improved. The patient could raise her right hand to the head and lift the left leg up from the right. She had

increased in flesh. About this time (August 1st)[1] she left the hospital and was taken to a boarding-house. Here, under the most unfavorable conditions, still greater improvement was made. All gastric symptoms disappeared; she had a ravenous appetite, and ate heartily of the plainest food. Bowels were regular; temperature normal; there were no fainting attacks, pains, or cramps. Menstruation began after an absence of eight months. Bones seemed to become harder, and thorax less elastic; the fractures in the femurs had apparently united. Crepitus disappeared; the legs could be moved without pain. Patient could move from one side of the bed to the other, and could sit propped up with pillows. Could use right arm freely, but motion in shoulders was restricted. She passed her time in sewing. The cough and expectoration continued.

In October it became evident that the disease was again progressing. The patient lost flesh; pain returned in the limbs; the fainting spells began; digestion was much disturbed, with marked tympanites, acid eructations, vomiting, and complete loss of appetite. The right femur became very sensitive, and the patient could no longer move about on the bed; and could lift the right arm only by the aid of the left. The mind was greatly depressed and irritable. At times there was slight delirium and sleep was disturbed. Toward the last of September, as mentioned, she began to pass small calculi, very hard, with sharp-pointed surfaces, causing intense pain before and after urination. She had previously passed a few at long intervals. By October 1st there was severe cystitis. Bladder was sounded for stone, but none found. There were numerous attacks of severe renal colic daily.

[1] She was observed after this time by my assistant, Dr. A. S. Warthin, to whom I am indebted for valuable assistance in the study of the case.

Menstruation had again ceased, and never returned. Changes in the thorax became more noticeable; the sternum seemed to have slipped down toward the abdomen; heart dulness displaced still further upward; the right clavicle was bent backward; the left leg was curved and drawn upward more than before.

From October to February, 1893, the condition gradually grew worse, though there were many periods when the patient seemed much better. The cystitis improved under treatment, and the gastric symptoms also; but there was much pain from the passage of gravel, and attacks of renal colic were of almost daily occurrence. In February she removed to a new house freshly papered and damp. She took cold, and from that time the disease made rapid progress. She could not make any voluntary movements except limited motion of the hands. Complained constantly of severe pains throughout whole body, especially in back. All necessary handling of the patient was exceedingly painful. Fainting spells were frequent, and patient became greatly depressed and fretful. Gastric symptoms became worse, and neither food nor medicine could be retained. There were frequent periods of collapse, with rapid, weak, and irregular heart. The passage of gravel and the attacks of renal colic increased. Cramps began in the muscles of the back, and kyphosis formed gradually. Two large bedsores now appeared, one on the sacrum, the other on the right leg, under the knee, where it pressed on the left. The thorax seemed more yielding. The right femur became soft and elastic. A loud systolic murmur developed over the heart area. There was decreased resonance over the left lower lobe of the lung.

On April 26, 1893, the patient, while complaining of severe pains in the back, had a fainting attack which ended fatally.

Treatment. During the first five weeks of patient's stay in hospital, treatment was wholly symptomatic. A concentrated syrup of lime was prescribed later, but as the gastric symptoms became so much worse, it was stopped. Phenacetin, quinine, and salicylates had no effect upon the pains, and did not reduce the temperature. The after-effects of morphine were so disagreeable and the general condition was made so much worse by it, that it was given but a few times. Codeine was given with good results, in the form of codeine phosphate, gr. $\frac{1}{3}$ p. r. n., the daily dose being from one to four grains. The pains were immediately relieved by this; the patient slept well; gastric symptoms improved; and there were no unpleasant after-effects. The temperature, which every day had ranged from 99° to 102° or 103°, fell to 98°–99°, and remained there with but two or three slight variations. This fall of temperature took place on the third day after the use of codeine was begun, and was permanent.

From this time until patient left the hospital, about eleven weeks afterward, codeine was constantly given; and all through this period there was constant improvement, as mentioned above. As gastric symptoms subsided, the concentrated syrup of lime, f℥j t. i. d., was given again. After leaving

the hospital the use of codeine (gr. $\frac{1}{2}$, at night) and syrup of lime was continued. In addition maltine with hypophosphites was given, f$\overline{3}$ss t. i. d. The diet was largely of cereals. Phosphorus, in doses of gr. $\frac{1}{100}$, was also tried; but the patient complaining that it caused stomach disturbance, it was stopped, and it was also necessary to discontinue the use of maltine and the syrup of lime on account of similar conditions. The treatment by chloral hydrate as recommended by Petrone[1] was also tried, fifteen grains being given t. i. d. for a month. Through all this time the condition became gradually worse. After this no further attempt was made to carry out specific treatment, and attention was given to the most important symptoms. Of these the renal colic received the chief attention, and was treated in every possible way, without great success. The calculi were constantly formed, and were passed in incredibly large numbers, often twenty daily, besides large quantities of sand. The patient became accustomed to the codeine, so that the dose was increased finally to eight grains daily; it then seemed to lose its effect, and during the last five weeks it was necessary, on account of the extreme pains, to keep the patient almost constantly under the influence of morphine.

Autopsy, two hours after death. No rigor mortis. Large amount of subcutaneous fat. Omentum well preserved. Diaphragm at level of third rib on the right, and third intercostal space on the left. Sternum soft, but partly calcified. Ribs can be cut through with a knife, but have thin shells of bone. They are much atrophied, the larger ones measuring 10 x 2 mm. on section, the cartilage just beyond the articulation measuring 13 x 5 mm., and not swollen.

Lungs partly distended. Left lower lobe collapsed; surface granular, pink, with small yellowish nodules (emphysema). Slight injection of bronchial mucous membrane.

Pericardium contains normal amount of fluid. White spot, size of dime, over right ventricle; several small cloudy spots on posterior wall.

Heart of normal size, lying one interspace higher than normal. Right ventricle contains small, soft, white clot continuous with a currant-jelly clot. Tricuspid and pulmonary valves normal. Left ventricle contains very long currant-jelly clot extending into auricle and aorta. Mitral and aortic valves normal; aorta narrow; intima smooth.

Liver slightly smaller, but otherwise apparently normal. Spleen 13 cm. long, 4 wide, 3 thick, anæmic and rather hard. Cut surface dry, glistening. Malpighian bodies show faintly; the trabeculæ increased.

Left kidney 11 x 4.5 x 4 cm. Pyramids anæmic, with small white specks (calcareous); also similar white specks, size of small pinhead, in the pale cortex. Pelvis contains numerous small calculi. Left ureter normal. Right kidney 10 x 6 x 4 cm. Contains numerous white specks like those in the left kidney in all parts; pelvis contains numerous calculi. Right ureter

[1] La Riforma Medica, 1892, No. 163, in Centralblatt für Bakt. u. Parasitenkunde, 1892, Bd. xii. p. 865.

dilated in its whole length. Seven small, hard, irregular calculi are lodged in its lower end just above the bladder.

Bladder contracted; contains two small calculi.

Uterus 5 x 3 cm.; pale. Tubes normal. Ovaries fibroid; $4\frac{1}{2}$ x $1\frac{1}{2}$ cm., white, anæmic, and nodular on the surface, with small cysts in the interior. The vessels of the ligaments show no abnormality.

All the bones of the pelvis are soft, cutting easily and breaking down like wet and rotten wood under the finger. The pubic arch on the same plane as the promontory, and distant from the latter 10 cm. The superior outlet of the pelvis of normal shape. The left acetabulum is lower down than the pubis, and points directly outward; the right one is in the normal position.

The bones of the upper extremities can be bent or indented by pressing the fingers through the skin, but are not deformed. The clavicles and scapulæ and the skull are hard and unyielding (as felt through the skin).

The bones of the lower extremities are all soft. The right tibia is broken just below the knee, and curved where it is crossed by the left.

Both femurs are strongly curved outward at the upper third; their heads are distorted and atrophied; the necks almost obliterated; the great trochanters higher than the head; the shafts irregularly thickened; the condyles distorted and atrophied. The right femur has fractures without evidence of callus at the upper third and the lower third, and another just above the condyles, which may have been made at the autopsy.

The left one has a fracture at the upper third, and one above the condyles, both probably made in getting out the bone. Under the periosteum just above the condyles on the anterior surface of the left femur, is a soft area 2 x 3 cm. in diameter.

The muscles of the thigh are very anæmic and yellow, especially close to the bone. There is also an unusual amount of interstitial fat.

The femurs were split longitudinally with a knife and show similar conditions on the whole, with slight variations to be mentioned.

The diameters of the right femur, which are not far from those of the left, are as follows: Head, 37 mm.; neck, 33 mm.; just below trochanter, 35 mm.; upper third, 30 mm.; middle, 42 mm.; lower third, 47 mm.; above condyles, 30 mm.

The head of the femur has a soft cartilaginous shell; the insertion of the ligamentum teres was pulled out in removing the bone. Within the shell is pale yellow fat, containing numerous fine spicules of bone.

The shaft is compressible throughout its length, deriving most of its strength from the periosteum. The neck and upper part of the shaft usually contain fatty marrow with variable quantities of spicules, filling in the whole width of the bone. On the outer side, just above the upper fracture, is a strip of pale-red marrow extending from the periosteum inward from $\frac{1}{2}$ to 1 cm. This also contains spicules of bone. Just below the great trochanter is a roundish mass, 15 mm. in diameter, having the color and consistence of

hyaline cartilage. It is continuous with the yellow marrow on one side, but free on the other, without having a definite capsule. On section this shows small cystic cavities, containing colloid substance.

In the middle of the shaft is a cyst, oval in shape, with diameters of 40 and 30 cm., lying obliquely to the long axis and reaching to the periosteum on one side. Its walls are smooth and translucent, hard to the touch in some places, but can be cut with a knife.

Above this are two areas undergoing cystic softening; below it several others of different sizes, the largest measuring 20 x 17 mm. in diameter. The smaller cysts contain unaltered blood (microscopic examination); the larger ones clear, odorless, oily fluid of neutral reaction. This did not give the chloride of iron and carbolic acid reaction for lactic acid, but was not tested otherwise.

The middle half of the shaft contains pink or red lymphoid and gelatinous marrow alternating, filling in the upper part of the bone cavity, from the periosteum, $\frac{2}{3}$–$\frac{3}{4}$ of the diameter; the outer $\frac{1}{3}$–$\frac{1}{4}$ being filled with fatty marrow. Both kinds of marrow contain the bone spicules described. From the lower third of the femur the inner part is made up of fatty marrow, continuous with that of the condyles. The widest part of the shaft is that containing the greatest amount of red lymphoid or gelatinous marrow. The former has a consistence, when fresh, varying from that of a fresh blood-clot to a normal, slightly hyperæmic spleen. The gelatinous marrow, darker red, has the consistence of œdematous connective tissue. The fatty marrow, including the parts in the head and condyles, is very anæmic.

The condyles have only a thin cartilaginous shell, filled with yellow marrow and trabeculæ, the latter being more numerous than those in other parts. Only in the part within the intercondyloid notch is there a small amount of red, gelatinous marrow.

The left femur presents changes on the whole like those of the right. It is, however, not so curved in the shaft. It contains also very few, and these small, cysts.

In the lower part of the shaft is a soft mass, just beneath the periosteum, measuring 2 x 3 cm. in diameter. On section this is dark red, resembling a blood-clot, but firmer; it is intimately adherent toward the centre of the bone to a firmer whitish (lymphoid) tissue.

The bones of the pelvis have hard but very thin plates of bone under the periosteum, but can be cut through with a cartilage knife. The space between the plates is filled with yellow, dirty-looking fatty marrow, traversed by spicules of bone and trabeculæ, some of which are as much as 2 mm. in diameter.

Owing to a misunderstanding the other bones could not be examined.

Microscopic examination. For histological examination I could use only the femurs, parts of the pelvis, and a piece of rib. These were examined fresh, and after hardening in Müller's fluid and in alcohol. The specimens hardened in alcohol were decalcified by Von Ebner's solution.

Femur. The periosteum is thickened almost everywhere, and has a fibroid structure with few nuclei.

The original compact layer of bone can nowhere be recognized. Immediately beneath the periosteum is a layer of fibrous tissue containing bony tissue in considerable quantity. This layer is usually from 0.5 to 1.5 mm. in thickness, but in some places, as near cysts, it extends further toward the centre of the femur. There is not a larger quantity, however, at the seats of fractures. The outer layer of bony tissue is made up of spicules of bone, which can best be examined by tearing out with forceps. They appear then as compound, branching processes, often perforated or forming meshes. The condition as regards calcification can best be recognized in the fresh state, or by pulling out splinters, rather than in sections.

Examined in this way it can be seen that the spicules are usually calcified, but not in their whole extent. Usually there is an irregular border on one or both sides, and sometimes the fibre is free from lime in its whole width for some distance, the margins of the calcified part being rather uneven. The calcified areas contain lacunæ and canaliculi, which are usually of normal appearance, though sometimes the lacunæ are large and the canaliculi few or absent. The calcified part usually shows distinct lamellæ. The uncalcified part is either homogeneous or finely granular, or less frequently coarsely fibrillated longitudinally. Occasionally it shows small lacunæ. Transverse perforating fibres cannot be distinctly seen.

These fibres or spicules, as stated, form part of the outer layer of the femurs, but they do not form a continuous layer, nor does their direction or the course of their lamellæ indicate that they are part of the original compacta, except in rare instances. This is true of transverse as well as longitudinal sections. The fibrous tissue in which they lie varies greatly in character in different parts. In some places it is dense and firm-looking; in others, soft, loose-meshed, or even having a myxomatous appearance. Long spindle, or oval or stellate cells lie rather sparingly in the fibrous tissue, and in some places there are collections of small round cells, occasionally cells resembling marrow cells (eosinophilous rarely), and at times polynuclear giant cells. Usually the fibres of connective tissue are parallel to the spicules, and present in sections an alveolar arrangement. This tissue is perforated by large but thin-walled vessels. In sections the structure of the bone spicules cannot be made out as clearly as in fresh specimens, but in sections made from preparations decalcified in Müller's fluid the so-called "carmine border" can sometimes be made out, corresponding to the decalcified parts described. In stained sections the bone corpuscles usually appear in the parts previously calcified, but they are often small and stain badly. In sections the edges of the bone fibres are usually smooth, but sometimes they are irregular, as if gnawed. Sometimes the edge of the fibre is lined by a thin membrane containing spindle-shaped nuclei, but typical osteoblasts cannot be found. Occasionally cells having the aspect of osteoclasts may be seen lying close to the edge of the bone.

Within this denser layer, but often passing into it gradually, is the widened marrow cavity with its different kinds of contents, as described above.

There are microscopic differences corresponding to the macroscopic ones. The simplest tissue is the yellowish part of the marrow. This appears under the microscope as fat tissue, with a varying amount of lymphoid marrow between the vesicles. The lymphoid material contains besides the ordinary small round cells a small proportion of eosinophilous cells, usually two or three times the diameter of a red blood-corpuscle, with a single round or oval nucleus. There are also in this part a few epithelioid cells with pale nuclei, and very rarely polynuclear giant cells. Bony spicules are rare in this tissue in the shaft.

The reddish marrow shows usually a small spindle-celled structure, containing large numbers of giant cells. These have from two to thirty or forty, usually more than eight to ten, round or oval nuclei in the centre or near one end of the body of the cell. The cells vary from 10 to 50 mm. in diameter, are usually round or short oval, but sometimes long oval. They are never of irregular outline like those in myeloid tumors. The nuclei usually stain deeply with nuclear dyes. The bodies take protoplasmic dyes well, but often have contents which affect the color, such as blood pigment or bits of osteoid tissue. In this tissue there is often an apparent structure, in that the spindle cells lie in whorls or form strands or rays, like those in a fibroid tumor. The giant cells often lie in the centres of such concentric masses. The tissue is well supplied with vessels, usually with thin muscle-walls, and contains more or less blood pigment. In this kind of tissue spicules of bone occur in various proportions. They are usually devoid of structure, are homogeneous, with few or no bone corpuscles. The sides are sometimes smooth, sometimes uneven, and occasionally have giant cells lying in spaces apparently excavated in them. These osteoclasts are precisely like the other giant cells described above.

The gelatinous marrow shows usually a very loose meshed fibrillated or myxomatous mass, with round, spindle, or stellate cells, and contains varying proportions of the elements just described as entering into the red marrow.

The walls of the cysts are made up of dense fibrous tissue, with trabeculæ of bone, sometimes in considerable quantity.

The cartilaginous tumor in the upper part of the right femur is made up of lobules of hyaline cartilage surrounded by fibrous tissue. The hyaline basis contains cells in large capsules; the centre of each lobule contains a softening cyst, the contents of which are sometimes colloid, sometimes finely fibrillated like young connective tissue, but without nuclei. In some of the lobules are small areas of calcification.

The tumor has no special sheath, but is continuous with lymphoid marrow.

The dark-red tumor in the lower end of the left femur is composed largely

of soft myxomatous or connective tissue containing osteoclasts. There are a few small bits of osteoid tissue, some of which are evidently undergoing absorption by the action of osteoclasts.

There are areas of small-celled infiltration in many parts, and several hemorrhages. Under the periosteum are small trabeculæ of osteoid tissue, some of which have fibrous ends. Large quantities of blood pigment occur throughout the mass.

The pubis has thin shells of hard bony tissue, sometimes perforated by absorption of the bone, but usually showing the original structure. This is irregularly decalcified and absorbed toward the inner part of the bone. The periosteum of the pubis is not thickened. The trabeculæ resemble those of the femur in being partly, or in some places wholly, decalcified. The marrow is fatty, with lymphoid infiltration in different parts. The pubis contains no osteoclasts and very few giant cells of any kind. Occasionally one, usually small and with few nuclei, can be found in the lymphoid tissue.

The cartilage of the acetabulum and the head and condyles of the femurs is usually smooth on the outer surface. In most places the decalcification has extended into all the trabeculæ continuous with the cartilage, but sometimes traces of the original structure can be found.

In the ribs decalcification has not been so extensive. The outer layer is usually complete, but decalcification extends irregularly into the compacta, and is advanced in the cancellous part.

Of the other organs, changes of importance were encountered in the kidney, spleen, and ovaries.

Kidneys. The kidneys contain extensive areas of small-cell infiltration in the cortex, and an increase of intertubular tissue with few nuclei in the pyramids. The infiltrations in the cortex are of varying size and shape, sometimes long and narrow, corresponding to the medullary rays, at other times irregular.

The epithelial cells on the whole are well preserved. Some tubules, in different parts, are dilated.

The capsules of Bowman are frequently thick and fibroid, sometimes having only a moderate thickness; sometimes the whole capsule is converted into a fibroid mass. The glomerulus capillaries are usually well preserved, but in some glomeruli some or all the loops are fibroid.

The arteries occasionally show thickening of the intima.

In various parts, especially in the tubules in the pyramids, are concretions, filling or even dilating the tubules, but without evidence of irritation around them. Concretions are also found in the cellular infiltrations, but not always.

Spleen. The spleen shows chronic hyperplasia, with increase of trabeculæ, but without increase of the lymphoid areas.

Ovaries. The ovaries have very few follicles. There are a few small cysts. Most of the tissue is made up of short spindle cells, in strands or rays, or firm connective tissue. There are few vessels. The vessels in the hilum seem normal.

The circumstances under which the patient was observed were so unfavorable for study that it is impossible to do more than mention briefly some of the points of interest involved.

The history of the case is not unusual, presenting as it does the common aspects of puerperal osteomalacia. In one respect the gross anatomical condition is interesting, namely, in the early and intense affection of the femurs. In the early fracture of the left one, and the prolonged lying in bed, we find the explanation of the absence of the typical osteomalacic pelvis—the beaked or heart-shaped pelvis. The difference in the consistence of the bones in the early and later stages, which led Kilian and others after him to distinguish *osteomalacia fracturosa* and *osteomalacia flexilis cerea*, is well illustrated by the early fractures and the gradual bending which took place during the last year of the patient's life.

Microscopically the changes found are those of a very advanced period, and bear out the ideas of recent investigators that the anatomical process is of a hyperæmic and inflammatory character. The inflammatory nature of the disease was asserted by Virchow (in his *Archiv*, Bd. iv., "Ueber Parenchymatöse Entzündung"). The theory is set forth by Von Recklinghausen in his exhaustive article, "Die fibröse oder deformirende Ostitis, die Osteomalacia und die osteoplastische Carcinose in ihren gegenseitigen Beziehungen" in the *Festschrift* Rudolf Virchow zu seinem 71 Geburtstage, etc. (Berlin, Reimer, 1891). It is interesting to see, also, that although regeneration of bone has taken place to a marked extent, the new tissue has in turn broken down, so that many of the changes found represent late lesions, or degenerations, of a process itself secondary.

The large numbers of osteoclasts found might at first sight suggest the idea that the primary dissolution of the bone was due to these, a fact considered of great importance by some, denied by others. Careful examination, however, makes it certain that these bodies are in reality disposing of tissues of little value and probably predisposed to destruction.

Study of the bones in various parts makes it doubtful whether we can believe that the origin of the disease is to be found in inflammation or hyperæmia, and leads us back to the view, unsatisfactory as it is, that changes of a more recondite kind, either changes in metabolism or disturbances in the normal processes

of breaking down and renewal of bone, lie at the basis of the disease.

As causes of the disease we find the commonest external conditions have been present in this case. The patient's own statement and that of her relatives threw no light on the subject, but it so happens that my colleague, Dr. Vaughan, saw the patient in her own home on the occasion of an outbreak of malignant diphtheria in the neighborhood. He describes the condition of the house and its surroundings as damp and unhealthy in the extreme.

The more direct causes of the disease which have been supposed at various times receive no light from this case. Now that the old theories of lactic acid, CO_2, and diminished alkalinity have been given up from insufficient evidence or contradictory facts, two theories remain. One is that of infection by bacteria, claimed by Kehrer, Petrone, and Latzko, for which there is no evidence and little probability, except that lent by the undoubted endemic nature of the disease in some parts, but even this is not constant, since localities once affected sometimes cease producing cases, as Ribbert has shown.

The other is that of Fehling (which includes the possibility of an assisting action in CO_2 or in diminished alkalinity), viz., that the disease is a tropho-neurosis, due to reflex irritation from the ovaries. The remarkable results of castration in osteomalacia seem to confirm this theory, but, while the facts cannot be questioned, there is a growing tendency to question the theory.

In many cases in which recovery followed the operation no abnormality could be discovered in the uterus, ovaries, or vessels.

Seeligmann, who had such a case (*Berliner klinische Wochenschrift*, No. 44, 1893, p. 1077), sees nothing in castration beyond the prevention of pregnancy and menstruation, but this does not seem possible in view of the number of cases in which neither of these were involved. I should remark here that in my own patient sexual desire seemed abolished, in striking contrast to the usual rule in osteomalacia.

The excretion of lime salts, the disposition of which in some cases is obscure, was very striking in my case, and its effects on the kidneys and ureters and bladder very important clinically and anatomically.

The results of the examination of the blood are of interest in connection with those of others recently reported.

Neusser (*Wiener klinische Wochenschrift*, No. 3, 1892, p. 45) found an excess of eosinophilous cells in the blood in a few cases of osteomalacia. In a case of senile osteomalacia, however, there was no increase of eosinophiles, but the blood contained myelocytes. He suggested the possibility of there being two forms of osteomalacia, differing in the manner mentioned as regards the blood. In a case cured by castration Neusser saw gradual decrease of the eosinophile cells. Rieder, however, found in one case only 3.6 per cent. of eosinophile cells, which cannot be looked on as an excess (*Beiträge zur Kenntniss der Leukocyten*, 1892). Sternberg in two cases found no increase of eosinophile cells and no myelocytes (*Zeitschrift für klin. Medicin*. Bd. xxii.). Tschistowitsch (*Berliner klin. Wochenschrift*, No. 38, 1893, p. 918) made careful examinations of the blood in osteomalacia and found no myelocytes. The eosinophilous cells varied greatly, but never exceeded 3.7 per cent. No effect could be observed on the number of these cells by castration. He found, however, that the lymphocytes were increased both absolutely and relatively, while the poly- and mono-nuclear cells were diminished. Tschistowitsch concluded, therefore, that besides the forms described by Neusser in which there is an increase of marrow elements in the blood, there is another form of osteomalacia with an increase of lymphocytes. I have been able to confirm the results of Tschistowitsch in my own case. The blood examined post-mortem shows 38 per cent. of lymphocytes, 52 per cent. of polynuclear cells, 9 per cent. of mononuclear and transition cells and less than 1 per cent. of eosinophile cells. There does not seem to me any reason for classifying cases of osteomalacia according to these peculiarities, as they are probably accidental, though it is important to have more observations on the blood, since it may be possible to learn something about the stage of the process as a whole from the alterations in the blood.

Diagnosis. Like all rare diseases, osteomalacia is frequently not diagnosed. Many text-books make it appear that in the later stages at least, the disease cannot be mistaken. This assumes a greater knowledge of diagnosis than is possessed by a large number of physicians, and it seems desirable that the differential points be

alluded to more frequently than they are in connection with diseases with which osteomalacia may be mistaken.

Even in Europe, in localities where the disease is not uncommon, cases are very frequently treated up to a very late period for other diseases. In my own case it seemed incredible that the nature of the affection had not been recognized before. Yet the patient was treated in a homœopathic hospital for other things at a time when the alteration in the right leg was progressing. I have strong reason for thinking that when the patient came to my clinic she did so at the instigation of a physician to get evidence in order to proceed legally against the physician who set the first fracture.

Sternberg (*loc. cit.*) has recently called attention to the difficulty of diagnosis and has given the important differential points to be sought for in distinguishing between osteomalacia and the diseases with which it is most easily mistaken. It is not necessary to quote these.

Osteomalacia is mistaken for some form of rheumatism more frequently than for all other diseases together. Much as the patient may think the pains rheumatic, a careful anamnesis and complete examination of the body would in most cases, except in the earliest stage, prevent error.

As regards treatment, the case teaches nothing new. The failure of the lime and the chloral was to be expected; they were given as experiments with very little hope of doing good.

I regret very much that phosphorus was not given a more thorough trial. Had I known of the result obtained by Sternberg (*loc. cit.*) I would have given the remedy in large doses, but in the light of the earlier reports I did not feel encouraged to continue it after I found the first administrations badly borne.

Phosphorus and castration must be looked on as the chief remedies in the disease, the indications for the latter being especially the possibility of conception or the existence of pregnancy and need of Cæsarean section.

Osteomalacia in North America. The peculiar distribution of osteomalacia in various parts of Europe is such as to suggest local causes and led me to examine the history of the disease in America (North). Cases of "mollities ossium," "malacosteon," "fragilitas ossium," and "osteomalacia" have been frequently reported in the

medical journals. I have examined all those under various headings in the *Index-Catalogue* and the *Index Medicus*, but find that but a small number can be considered as genuine cases of ostomalacia. Most of them are cases of osteomyelitis, caries, tuberculosis, sarcomatosis, cancer, or fragility.

The first report was made by J. W. Tenny, in 1839 (*American Journal of the Medical Sciences*, 1839, xxvi. p. 506), under the title "A Case of Mollities Ossium." The patient was a married woman of forty-three, the mother of five children, eighteen months past the menopause, living in Webster, Mass. The disease lasted two years, during which time the bones became so soft as to be easily bent. Autopsy showed changes similar to those of osteomalacia.

In 1861 W. H. Lamme, of Centreville, Ohio, reported "A Case of Mollities Ossium" (*Cincinnati Lancet and Observer*, vol. iv., 1861, p. 215) in the person of a married woman of sixty-three, the mother of several children. Illness lasted for ten years, with progressive deformity and softening of the bones of the lower extremities and severe pains. The bones were "as soft as bags filled with hair." No autopsy.

N. Dalton reported a case seen in Ohio, in 1860, under the title "A Cure of Mollities Ossium with Calcium Phosphate and Phosphoric Acid" (*Trans. Ohio Medical Society*, Cincinnati, 1863, xviii. p. 67). The patient was a female, seventeen years old, unmarried. She was ill two years, with progressive softening and deformity of the bones of the pelvis, ribs, clavicles, cranium, and legs, with intense pain and spontaneous fractures. In this case the urine contained "a large quantity of whitish-gray deposit equal to one-third of its volume." Dalton found this urine contained over eleven grains of earthy phosphates in two ounces. Under the treatment indicated in the title, the bones became solid and the excretion of lime ceased.

Joseph Jones has reported a case of a white girl who died at eighteen years with a condition resembling osteomalacia (*Medical and Surgical Memoirs*, by Joseph Jones, New Orleans, 1876, vol. i.). The patient lived for a time on an island in the Ohio River, in extreme poverty and most unfavorable hygienic conditions. From the age of five there was progressive softening of the bones, with great pain.

Bolles reported a case of "Remarkable Fragility of Bones" (*Boston Medical and Surgical Journal*, 1871, vii. p. 181), which was probably one of osteomalacia. The history is incomplete. Multiple fractures from slight causes, with union and breaking down of callus, were observed for two years after the menopause in a married woman of forty-six.

The word osteomalacia first appears in connection with a case reported by Ellis, in 1878 (*Boston Medical and Surgical Journal*, 1878, xcviii. p. 5). This was the case of a man of fifty, who died after an illness of ten months' duration, with fractures, pain, etc. It does not seem that this was a case of osteomalacia, though the reporter could find no evidence of "cancer, caries, or leukæmia."

In 1883, Stone reported a "Case of Osteomalacia with Autopsy" (*Boston Medical and Surgical Journal*, 1883, cix. p. 220). Married woman of fifty-five years, mother of six children, had rheumatic pains, followed by progressive softening of bones, with fractures and deformity, lasting four years. Autopsy showed characteristic changes.

In 1887, Lamb, of Washington, reported a case of osteomalacia (*Journal of the American Medical Association*, 1887, viii. p. 493). Woman aged sixty-eight, single. Ill twenty-one years, with extreme pain in legs, weakness, "drawing-in pains," softening and deformity of bones. Autopsy.

Wheaton reported the case of a single woman of thirty (?), still living at the time of the report, who for four years had softening of the bones with deformity and fractures. The urine was sometimes milky, containing an excess of phosphates (*Northwestern Lancet*, 1891, p. 389).

Wheaton refers to a case in the care of Dr. Briggs, of St. Paul, which does not seem to be reported otherwise.

Woman of thirty-five years, married. After the birth of her fourth child softening and deformity appeared in the spine and pelvis. Ovariotomy was performed, but the disease continued to progress.

The case of French (*Northwestern Lancet*, 1891, p. 413) does not seem to be one of osteomalacia, but rather of malignant disease. The case of Russell (*Cleveland Medical Gazette*, 1892, vii. p. 471) also seems doubtful.

Finally, in 1892, Lamb gave the history of a case, the bones of which are in the Army Medical Museum (No. 10,010) (*Journal of the American Medical Association*, 1892, xviii. p. 188). Female, single, aged sixty-nine years. Following acute arthritis there was progressive deformity and softening of the bones, lasting twenty-six years. The autopsy showed traces of old pelvic inflammation.

Excluding the doubtful cases of Ellis, French and Russell the total number of those reported is only ten; all of the cases were females and whites.

Three of the cases occurred in Massachusetts, two in Ohio, one on an island in the Ohio River, two in Minnesota, one in Virginia, and one in the District of Columbia. All the patients seem to have been of American birth.

Almost nothing is said of the family history. In four cases the environment is not mentioned; in three cases it was considered good. One lived in great poverty on a low island subject to overflow; another lived very sparingly; and in the third the disease began after a period of exposure and privation while nursing in the army.

Concerning the previous history of the cases very little is said. In four it was stated to have been good; one was chlorotic; another had prolonged malaria; and several had histories of rheumatism or arthritis aside from that connected with the disease. In five of the cases the subjects were single and had borne no children. In four the disease began after the menopause; all of these cases had borne children with apparently normal deliveries and recoveries, all of them having large families—five to ten children. The one puerperal case occurred at the age of thirty-five after the birth of the fourth child. In the chlorotic patient the disease seemed to increase in severity at the time of the menstrual flow; in the case of Jones, menstruation was long delayed and only established under treatment.

The duration of the disease varied from two to twenty-six years. The longest duration was observed in the oldest cases. Four of the cases were living at the time of the report; in three of these the disease had lasted about two years; in the other the duration was not given. Of the 7 fatal cases 1 lasted two years, 2 four years, 1 ten, 1 thirteen, 1 twenty-one, and 1 twenty-six.

During the greater part of these periods the patients were helpless in bed.

In all the cases the disease began with rheumatic pains, so that a diagnosis of rheumatism was usually made; in one case the diagnosis was influenza. The intense and deep-seated pains began usually in the lower extremities, and in all but one case form a striking feature of the disease. These pains are described as "crushing," "drawing," etc., and were increased during bad weather. Associated with the pains were progressive weakness; fractures from slight causes, usually not uniting; increasing softness and deformity of bones; and finally complete helplessness. Appetite and digestion were usually good; in one case obstinate constipation; the mind remained clear, and nervous symptoms were not marked. In three of the cases dyspnœa from pressure upon the thoracic organs was prominent as a late symptom. Death occurred usually from exhaustion.

The condition of the urine is mentioned in but five cases: in one it was said to be normal; in three increased in amount and depositing a greatly increased sediment of phosphates, in one case one-third of the volume; in the other case it was "loaded with urates" (?).

The blood was not examined in any of the cases.

In four cases only was an autopsy held. In all of these there was great deformity of the bones, atrophy, and fatty degeneration of muscles. The bones of the extremities, pelvis, and spine were so softened as to be easily cut or crushed; in some places bone was completely absorbed and no trace of it found. The compact portion was greatly thinned and softened, the medullary spaces widened and the marrow increased, dark-red "like coagulated blood," easily cut, consisting of "blood-cells and vessels," "fat-cells and free fat," or of "plates and fibres loosely held in a whitish mass of fat or gelatinous matter;" some portions filled with liquid fat.

No tests were made for lactic acid in the bones or urine.

In one case ovaries were normal, in two they were atrophied, and in one case not mentioned.

In two cases small calculi were found in the kidney.

This summary shows that the general features of osteomalacia

were present in these cases, although they differ in many respects from those observed in other countries. Gelpke, in his monograph on the *Osteomalacia in Ergolzthal,* near Basel (Basel, 1891), states that in countries where osteomalacia is not endemic the non-puerperal forms are seen more frequently than puerperal cases, a point which Ribbert ("Anatomische Untersuchungen über die Osteomalacia," *Bibliotheca Medica,* Cassel, 1893) questions, but which the cases so far reported in this country seem to bear out.

THE MILD CHARACTER AND DIMINISHED PREVALENCE OF SYPHILIS, AND THE INFREQUENCY OF VISCERAL SYPHILIS.

By J. H. MUSSER, M.D.,
OF PHILADELPHIA.

The writer is fully aware of the absence of the precision of statements in this paper which should attend all scientific communications. For reasons which will be briefly considered later, such precision could not be obtained. It is unfortunate that we must deal in generalities, but the tide of thought may be turned in the direction indicated by these lines, and precision sooner or later attained. The paper is presented with the object of eliciting discussion, so that, if possible, we can carry with us, if desirable, more definite notions of the prevalence of the disease and the virulence of its manifestations.

The frequency of a disease of the character we are considering in a community can only be determined positively by compulsory notification. In the absence of such notification, we must resort to the statistics of the hospitals of the community, and to the records of physicians in private practice. The former do not tell the story correctly, because too many individuals are engaged in the make-up of the statistics. That uncertain quality, the "personal equation," is one of the many discordant factors which make such data unreliable. Moreover, the victim of a disease like the one under consideration, which presents so many "ups and downs," may be treated at different times in the same institution during the same year, or at various institutions in that period.

The records of physicians in private practice would likewise be misleading. The tendency of this class of patients to see more than one physician, the choice depending upon the organ or structure at that time the seat of the disease, is one factor. Again, the

class of practice which engages the attention of the physician would modify his statistics. The specialist on venereal diseases sometimes shudders at their apparent prevalence in the community, while the general practitioner observes but few cases in a corresponding period. Then, too, a man at fifty must not decide upon the frequency of a disease because he sees more than he did at twenty-five.

In short, there is no definite quantity upon which to base our calculations. This may be secured in part by taking a definite class of men who are under the observation of a corps of students guided by the same definite purpose, both classes remaining as more or less fixed quantities. The statistics of the Army or Navy are therefore reliable up to a certain point. They are not, however, an index of the ravages in a community.

Another factor that does not fluctuate may be derived from the records of the hospitals and dispensaries which treat venereal diseases alone. If one only of each existed in a city, a fair idea of the prevalence of the disease could be obtained. Usually this is impossible; especially is this so with dispensaries, for the patient wanders from one to another at his own sweet will as fancy or convenience dictates. Many factors also, as the movement of population, cause a variance in the attendance of patients upon a particular dispensary.

The nearest approach to the ideal definite quantity is to be found in a community which has only one hospital for the treatment of the disease under consideration. Even here fallacies enter, and we can only judge of the frequency of the disease by inference, for the class attendant upon the hospital are only a portion of the community which may be infected.

Obviously, therefore, we can only come to that which approaches a conclusion by the expression of individual impressions. Scientific definiteness of statement, it is to be deplored, cannot be obtained. If such impressions tally with the statistics of a hospital situated under the circumstances above indicated, they are all the more trustworthy.

Notwithstanding the increased scope of view, and the occurrence of fallacies, the writer is firmly imbued with the impression that there is less syphilis in the community in which he resides than there was ten or fifteen years ago. It is certain that the

disease does not come under observation as frequently, either in private or hospital practice, as in former years. Does this tally with hospital statistics which have some impress of definiteness?

In Philadelphia the treatment of syphilis with lesions which render the disease communicable is limited to the Philadelphia Hospital (Blockley). To the wards of this hospital are admitted the poor classes that are victims of the disease. It follows that any statement concerning the prevalence of syphilis obviously applies only to this prevalence among the poorer classes. The development of the disease under discussion is, however, more favored by the conditions that surround this class. Any fluctuation in the tendency of the disease among them is nevertheless a tolerably fair index of its frequency in a community.

The percentage of the cases of syphilis treated in the Philadelphia Hospital is indicated by the following table:

Per cent. Syphilis in Hospital for Periods of Five Years—1864 *to* 1893 *inclusive.*

1864 to 1868 = 6.68 per cent.	1879 to 1883 = 4.26 per cent.
1869 to 1873 = 4.56 "	1884 to 1888 = 3.76 "
1874 to 1878 = 3.36 "	1889 to 1892 = 3.05 "

It is thus seen that the reduction of the percentage of cases of syphilis is to less than one-half, and in the face of the fact that the population of the community from which the cases are drawn has increased fully 35 per cent. in the three decades, and that, moreover, this reduction of percentage would be still greater if the other wards of the hospital increased in a ratio corresponding to the increase of population of the city of Philadelphia. In 1864, 5815 cases were treated in the hospital, whereas it had only increased in 1892 to 7942 cases, a ratio of increase far below the increase of the sick poor of the population. This increase did not occur, because five new hospitals were built and all the old hospitals enlarged since that time, furnishing shelter for the sick, who otherwise would have sought the Philadelphia Hospital.

The cause of the diminished prevalence of syphilis can only be a matter of speculation until we have more satisfactory knowledge of the nature of the specific virus and of its biological properties. It is fair to presume that the increase of the habits of cleanliness of the public is one large causal factor. Then, too, the more modern methods of treatment, which lessen the duration of the contagious

period of the disease, contribute to this decline. It is not, however, stretching the imagination to any great extent to urge the probability either that the soil is less favorable for the development of the disease, or that the activity of the virus is attenuated.

It, of course, must be remembered that the "war period" must have had much to do with the prevalence of syphilis in the decade from 1864 to 1874.

The mild character of syphilis. I have had forty-eight cases of syphilis throughout its course, under observation as family practitioner, for a period of ten years. Three are women who have married and have had children. Children were born in the course of the disease of two of the mothers with symptoms of inherited syphilis, but have grown to healthy children since their birth. Other children in perfect health have been born to the parents. All of the cases above noted I believe are cured. None of them ever presented grave lesions of syphilis. The only case of death from syphilis that I saw, barring aneurisms and other vascular lesions of this disease, was a case of meningitis which developed in a young man in the practice of Professor Wood. If we compare the records of the venereal wards of the Philadelphia Hospital of twenty and thirty years ago, we find the most marked improvement. Formerly, grave ulcerative lesions of external syphilis were common; now they are the exception. The "syphilitic cachexia" was frequently seen; now it is extremely rare. I had expected to show from a study of all cases of syphilis in the hospital a decline of the tertiary varieties of the disease. Such decline has occurred, and in view of the facts previously mentioned regarding the increase of accommodations of other institutions for such patients, is not without significance.

From 1864 to 1868, 3 per cent. of all cases in the hospital were recorded as tertiary, visceral, or nervous forms of syphilis. All forms of internal syphilis are included.

The diminution was one only of moderate degree—1868 to 1873 to 2.25 per cent.; 1874 to 1878, 1.95 per cent.; 1879 to 1883, 2.2 per cent.; 1884 to 1888, 2.65 per cent.; 1888 to 1893, 2.45 per cent.

The decline is only a fractional one, but even no decline in per cent. would mean a diminution in amount. I believe there was

less tertiary syphilis than the records indicate. In one year the records of the nervous wards showed sixty-nine cases of syphilitic hemiplegia; in another year the cases of this character were less than six. It looks as if the diagnosis was made in accordance with the bias of the observer. The small amount of tertiary and visceral syphilis seems to indicate a lessening of the virulence of syphilis. This is substantiated by the accounts of the disease given by writers of forty or sixty years ago, and by the statement of physicians whose experiences bridge the epoch just mentioned. In the Presbyterian Hospital we have treated in the medical wards 9000 cases. Of that number thirty cases are diagnosed as tertiary syphilis; eleven cerebral; two spinal; two hepatic; four laryngo-pharyngeal; a total of forty-nine cases. Certainly if the disease was common and severe, more cases would have resorted to this institution.

Syphilitic disease of the organs of the thorax and abdomen is considered, with the exception of syphilis of the bloodvessels, endarteritis. Here, again, older writings are full; modern writings are the echoes apparently of the past. The experience in the Presbyterian Hospital is a case in point of their infrequency. In a series of three hundred and thirty autopsies which I have conducted, the visceral lesions of syphilis (other than vascular) occurred but once. In private practice, I have had but two cases (elsewhere reported) of visceral syphilis outside of the nervous and vascular system. Are we not justified in asking, if pulmonary or other forms of visceral syphilis are rare, is it not possible that so-called syphilitic lesions of the arteries and nervous system are due to other causes?

The statistics of the hospitals which I could consult are unreliable, I regret to say, and any information they may possess is buried in such a manner in the notes of the autopsy, as to render them inaccessible.

Granting the mild character of syphilis and the infrequency of visceral forms, are we warranted in considering the syphilitic process as a factor in the pathology of vascular and nervous syphilis? I believe visceral syphilis was common in the past, or else mistaken for the lesions of tuberculosis. I believe it is at present infrequent, without being able to give definite data. Should there not be a

similar decline in the frequency of vascular and, secondary to it (for there is usually a primary endarteritis), nervous syphilis?

Résumé. In the Philadelphia Hospital, the only institution in Philadelphia in which early syphilis is treated, there has been a progressive diminution in the number of cases of syphilis, notwithstanding the increase in the population of the community. This statement is made notwithstanding the statistics were begun just after the war, in time rife with such diseases. It is at present a mild disease. Tertiary manifestations are not common. Visceral syphilis is rare.

DISCUSSION.

Dr. E. G. Janeway: I would perhaps admit part of the conclusions in Dr. Musser's paper, those derived from statistics; and yet I think it would be a mistake if we should overlook syphilis as a factor in the production of disease. In what I have seen of locomotor ataxia and general paresis, I am led to believe that syphilis stands in a very strong etiological position as regards the development of those diseases. In coming to a conclusion in this matter, as regards the infrequency or decreased severity of internal syphilitic affections, one would have to ascertain if these diseases were becoming infrequent, and in what relation syphilis stood to them. My own opinion is that it is a strong factor in the development of locomotor ataxia, and still stronger in general paresis. Then, again, the fact is that quite a number of general practitioners fail to take up syphilis as a producer of internal disease. Certainly in diseases of the nervous system we see it; and I think it is a general rule now, in obscure cerebral affections to try the treatment by potassium iodide and mercury in order to exclude syphilis.

With reference to syphilis in the interior of the body, it is not so very infrequently that syphilis is present when it is not thought to exist; and it may occasion symptoms which simulate phthisis. We have met with four cases of this kind where there was fever and pain and wasting, and, this fever stretching over a considerable period of time, these patients were supposed to be consumptives. They were sent to health resorts, but failed to be improved. Finding some history or lesion of syphilis, they were put upon anti-syphilitic treatment, and commenced to improve in the city of New York, when they had not improved in the Adirondacks and other health resorts. One patient had first been in a health resort; had been condemned as a case of general tuberculosis; had had a fever which kept up for three months, together with a cough, and had gradually wasted. No bacilli were ever found in his sputum. After two and one-half years he came to see me

again the other day with a swollen knee-joint. He had improved on anti-syphilitic treatment, and this knee-joint trouble yielded to iodide of potassium.

I have seen the same thing take place in a case of enlarged nodular liver which was supposed to be cancerous, and treatment with iodide of potassium caused the man to increase in weight from 150 to 200 pounds, which was his original weight.

Such cases show that we must not leave out of account in our consideration of the etiology of visceral diseases the factor of syphilis.

I might say that in my judgment syphilis undoubtedly stands very strongly as an etiological factor in the development of aneurisms. We find the proof of this in the histories of patients with this complaint. Syphilis also is to be considered as a cause of arterial and also of heart disease at times.

Dr. H. M. Lyman: I am very much interested in this paper of Dr. Musser. It is a line of investigation that needs to be followed out much more extensively than has been done heretofore. My own investigations with regard to the prevalence and severity of syphilis at the present time are quite in accord with those that have been expressed by the paper. In conversation with physicians practising in the Hawaiian Islands and in other islands of the Pacific where syphilis was introduced during the last century, and where its ravages were of the most terrible character, I learn from them that syphilitic manifestations are different at the present time from what they formerly were; that the disease has assumed a very much milder and more tractable form, and that there is frequent absence of the severe ulcerative and cachectic characteristics that used to be common features of the disease. I think we are safe in assuming that where a population is becoming more stable in its constitution and more civilized in its character, there the virulence of syphilis is diminishing. We notice that wherever the outbreaks of syphilis were conspicuous in the history of the world, they have occurred at times when there was great instability in the constitution and movement of population, and where people from different parts of the world were being brought violently into contact with one another under most unfavorable hygienic conditions. Then, too, we find that the tendency of syphilis is to a diminution in the virulence of its primary and secondary manifestations. My experience is exactly in accord with that of Dr. Janeway in this matter. So true is it that the primary and secondary manifestations are often insignificant, that whenever I meet with a case of locomotor ataxia or of paretic dementia, it is my universal habit to ask the man at once, "When did you have a sore?" Though the patient almost always acknowledges the existence of a venereal sore, I have been surprised to see how rare was a confession of secondary symptoms as consequences of such sore. The questions as to eruption, sore mouth, etc., would almost invariably elicit a denial of such lesions, and yet the original sore would always be freely acknowledged. Yet these later manifestations of

disease, such as tabes and paretic dementia, which are most closely related to syphilis, if not an actual manifestation of late forms of syphilis, are exceedingly apparent. My impression is that the disease is really subsiding in virulence. That it tends to become extinct is proved by experience in the Pacific islands. When first discovered by European voyagers those islands were found to be free from syphilis. The inhabitants were the direct descendants of emigrants from Asia. On the Asiatic Continent syphilis has always been rife; but those people, the descendants of a syphilitic population, were universally free from the disease. Now, I can account for that only by the supposition that these people, having been lost in the Pacific, and having become domesticated and completely isolated from the rest of the world, gradually lost their syphilis, the disease becoming attenuated, and in the natural course of events becoming extinct during the course of transmission from generation to generation, so that at last there was a population entirely free from the disease until reinfected by the arrival of European discoverers.

Dr. I. E. Atkinson: It is difficult to discuss a paper based upon statistics without statistics to place against them. It seems to me, however, that it can hardly be proven that syphilis is becoming less prevalent from an observation of only thirty years. I think we will admit that syphilis is not so severe a disease now as at the end of the fifteenth century; but there are so many circumstances that may interfere with statistics that are based upon the records of a single hospital, that we must be careful in drawing conclusions from them. For example, Dr. Musser refers to a first series of observations taken at the time of the great war, when there was an enormous dissolute floating population, which would very readily account for the large percentage of syphilitic cases in the hospitals then. Again, the differentiation between syphilis and local venereal ulcers was probably not as clearly understood at that time as it is now. Then, again, the statement that tertiary syphilis is so much less prevalent than it used to be is one that is only shown by a very small percentage. Now I have no statistics at the present time to place against these, but I know that so far from looking upon syphilis as a disease that tends to become insignificant in a small space of time, I am still in the habit of seeing in our hospital wards grave syphilitic disease, and constantly having patients with grave nervous and visceral disease due to this infection. I do not think that the claim that syphilis is a disease that is becoming milder within the observation of the present generation, should be taken except with a considerable degree of allowance.

Dr. Post (of Boston): I am very much flattered by the kind invitation of your President to take part in this discussion. I came in to listen rather than with the expectation of saying anything. The title of the paper attracted me in the first place, because it indicated an experience which was entirely foreign to my own. I am constantly seeing more and more syphilis, and graver and graver cases. It is, of course, possible that this is

due to the fact that my position as a teacher of syphilis directs such cases to me. The number of cases of primary and secondary syphilis that appear in the Boston Dispensary is, I am sure, not diminishing in the least. It seems to me that, on the contrary, it is increasing in this particular clinic, and I cannot help wondering if in Philadelphia, if the statistics of the whole city could be taken into consideration, we should not find that cases of primary syphilis had disappeared from one hospital and had increased in number at another hospital or dispensary.

I have within a little while heard cases of diphtheria divided into three classes: first, a class in which the cases were so mild that under any treatment or no treatment they would get well; a second class, in which the cases were fatal from the very beginning; and a third or largest class, in which the cases were severe, but in which treatment showed itself of value. It has occurred to me that cases of syphilis may be divided in somewhat the same way. There is a very large number of cases in which the disease is extremely mild; there is also a small class of cases of great severity from the very beginning, the cases which might be called "galloping," which are known by the French as cases of early malignant syphilis; and then a very large number of cases in which treatment is certainly of the very greatest value. I cannot help thinking that it would be possible for any one man to see a long list of cases of the first character, in which syphilis was mild, and he might form his opinion that this disease was at the present time an extremely mild one. I am sure that for a long series of years I saw such a class of cases; but latterly I have been in the way of seeing the cases that have gone to the bad in spite of treatment; in other men's hands they have failed to do well, and many of them, I regret to say, have continued to do ill under my own observation.

It seems to me impossible that syphilis should be dying out in our country, considering the way in which we cultivate the disease. In my own locality there is absolutely no control exercised. It must be the rarest thing for the prostitute to continue her way of living for any great length of time without becoming syphilized, and then instead of offering her an asylum or of attempting to help her to get well, she is practically obliged to take refuge either in an almshouse or to gain admission surreptitiously—that is, for some complication—to one of the regular hospitals, or to beg or starve. Some of them certainly have a conscience about the matter and attempt to abstain from spreading the disease, but there comes a time when there is a choice between starvation or the continuation of her old life, and there are very few women who are able to face starvation for the benefit of mankind.

I cannot help wishing that the statistics, of which I only heard a very small part, may prove to be true, but I fear that there must be some other factor which Dr. Musser has failed to take into consideration.

THE COMPENSATORY CHANGES IN THE RIGHT VENTRICLE IN MITRAL STENOSIS.

A Case with Hypertrophy, but without Dilatation; Death from Hæmoptysis.

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J. K. C., aged thirty-five years, financial manager of a large printing business. As a lad he was not very robust, but was never seriously ill. There is a probable history of rheumatism; no chorea. As he grew to manhood he became anxious about his health; had the morbid sensitiveness so often occurring with bad digestion. He cultivated art and literature. He took careful and systematic physical training, being especially fond of fencing, at which he was an expert, and indulged regularly in the exercise, but always with careful moderation. He had a splendidly developed chest. He first came to me for advice in July, 1889. Some years prior to that time he had become aware that he had organic disease of the heart, probably in seeking advice for pain in the lower præcordial region caused by imperfect digestion. This discovery caused him much mental worry, and he sought advice in many quarters—from all sorts of men, from the most eminent physician down to the most nefarious quack.

In July, 1889, there were well-defined symptoms of stenosis of the mitral orifice; loud, harsh, presystolic murmur; synchronously a fairly marked thrill; no displacement of the apex impulse; no signs of enlargement of either left or right ventricle. There were no respiratory symptoms or complaint of shortness of breath, unless undue exertion was made. The digestion was very bad, there being much flatulence and constipation. He was greatly depressed mentally, attributing his ill health to the heart disease. He was assured that the heart was, for the present, blameless—that the cause lay with the digestion—and appropriate treatment was prescribed. He was advised to continue regular fencing and other exercise in moderation. This he was able to do for over a year.

In January, 1891, he had a severe attack of influenza, with considerable bronchitis. In May following he had pneumonia badly, one lobe being

involved at first, and a second lobe as he was convalescing. Throughout both these illnesses the heart stood the strain perfectly, the only untoward symptom being free hemorrhagic sputum in both the bronchial and pneumonic attacks. After a somewhat tedious convalescence he resumed business, and continued at it until 1893, with short and more frequently recurring interruptions from attacks of bronchitis, during which the sputum became increasingly hemorrhagic. The breathing became shorter, so that fencing and all physical exercise had to be abandoned.

During this time the præcordial thrill became more marked and the murmur louder and more harsh, and occupied the whole of the diastolic period; it was somewhat louder at the beginning than at the middle, but loudest at the end of the period. Both sounds were distinct at the apex and also some distance beyond it.

In the last week of February, 1893, he took cold, and had a sharp attack of bronchitis, with much cough and muco-hemorrhagic sputum. In ten days he went to the office for an hour, but the cough grew worse afterward. He then remained at home, moving about the house. On Saturday, March 11th, there was slight fever, and he was feeling very apprehensive as to the future. On Sunday evening he was somewhat better; but he expressed a determination to sit by an open fire all night. One hour later a fit of coughing came on, with profuse hemorrhage, and he expired in ten minutes.

At the *autopsy* the lungs were found very large and crepitant throughout; they contained many minute calcareous nodules, but no infarcts. The pulmonary artery was dilated and atheromatous to its smallest branches. The point of rupture occurred in the right lung, but could not be found. The right ventricle was contracted and empty; greatly hypertrophied; its tissues firm, forming the apex of the heart, and looked like a normal left ventricle; there was no dilatation. The left ventricle was considerably atrophied and its tissue dark and friable. The left auricle was greatly dilated. The mitral orifice, a slit-like opening, was one centimetre in the long diameter. The posterior mitral segment was extremely calcareous. The valves were competent. Other organs were normal.

The noteworthy features in this case are the unusual duration and the massive hypertrophy and absence of dilatation of the right ventricle. We have no accurate data by which to determine the exact duration; but it must have been fifteen, and probably twenty years. Rosenstein[1] says that—

"Compensation is brought about by the right ventricle alone, and may suffice to sustain life endurably for years, and exceptionally for even more than ten years. But we must not forget that such cases are of an extremely exceptional order."

[1] Ziemssen's Encyclopædia, vol. vi. p. 131.

Then, such persistent compensation in mitral obstruction is extremely rare—a compensation so powerful as to actually lead to a fatal termination. Had it begun to fail life might have been prolonged for some considerable time.

The persistent competence of the heart led to a more favorable prognosis than was justified by the results.

Of Broadbent's[1] useful division of the history of these cases into three stages, Mr. C. did not reach the end of the first, in which the first and second sounds as well as the murmur are all heard at the apex and the second sound also to the left of the apex. In this stage, according to his experience, there are no symptoms. That is, it is not till cardiac failure sets in that symptoms show themselves; and cardiac failure occurred in all his cases.

The constant failure of the right ventricle in mitral stenosis is doubtless due to the recurrent attacks of rheumatism that occur in such cases. With these attacks of rheumatism there is always an accompanying anæmia that usually persists during the intervals between the rheumatic attacks and prevents the proper nutrition of the heart.

Then there is rarely any effort made to develop the heart to meet the altered conditions by systematically "training" the cardiac muscles. Most of the subjects of mitral stenosis are females; and no thought is given to their physical training, especially with a view to strengthening the heart. Mr. C.'s case well illustrates the benefits to be derived from persistent systematic physical training, as, no doubt, the complete compensation in his case was largely due to the exercise of fencing—an exercise taken in loosely-fitting garments and in well-ventilated rooms. There can be no doubt that much good would be done in all cases by systematic, graduated exercise taken in the intervals between the attacks of endocarditis. Not only would the heart be strengthened, but the general health would also be improved, and the tendency to the recurrence of rheumatism lessened. There is probably no form of heart disease that can be more beneficially influenced by "training" than mitral stenosis.

As to compensatory cardiac changes occurring in mitral stenosis

[1] Harveian Lectures, Brit. Med. Journ., July, 1884, vol. i. p. 149.

there is a diversity of opinion among the authors of the various works on medicine, and, unfortunately, many of them are inaccurate. Thus Aitkin says the right ventricle is dilated and hypertrophied, and Niemeyer does so likewise. Flint[1] is not clear in his statement, in one place speaking of hypertrophy and dilatation, and a little further on of hypertrophy only of the right ventricle as compensating for the obstruction.

Strümpell[2] says:

"The right ventricle can, by more work, so increase the pressure in the pulmonary vessels that, in spite of the narrowed orifice, an approximately sufficient quantity of blood may pass into the left ventricle. Hence we find in mitral stenosis a very marked hypertrophy and dilatation of the right ventricle."

Loomis[3] is less definite, but thinks—

"That mitral stenosis admits of but slight compensation . . . . and that obstruction in the pulmonary circulation may lead in time to dilatation and hypertrophy of the right ventricle."

Shattuck[4] says:

"So it is in the right ventricle that compensatory increase in power must chiefly be sought. This portion of the heart is, therefore, dilated and hypertrophied, the wall at times acquiring a thickness equal to that belonging normally to the left ventricle and displacing the latter in the formation of the apex."

Osler[5] writes thus:

"Eventually the tension is increased in the pulmonary circulation, owing to the impeded outflow from the vein. To overcome this the right ventricle undergoes dilatation and hypertrophy, and upon this chamber falls the work of equalizing the circulation."

Pepper[6] says:

"Finally hypertrophy and dilatation of the right ventricle supervene, and seem to maintain the proper circulation. The right ventricle is never capable of as decided and persistent hypertrophy as is the left."

[1] Practice of Medicine.
[2] Text-book of Medicine, p. 285.
[3] System of Medicine, Pepper, vol. iii. p. 682; also Practice of Medicine, p. 489.
[4] Reference Handbook of the Medical Sciences, vol. iii. pp. 587, 588.
[5] Practice of Medicine, p. 615.
[6] American Text-book of Medicine, vol. ii. p. 288.

Lyman,[1] in his late work, writes:

"As a consequence of this condition the right ventricle becomes dilated and hypertrophied."

Thus it is seen that there is general agreement among American authors that the compensatory changes in the right ventricle consist in dilatation as well as hypertrophy. On the other hand, English authors, as a rule, regard the compensatory changes in the right ventricle in mitral diseases generally as consisting of hypertrophy only, and look upon dilatation as evidence of failing compensation.

Thus, Sir Walter Foster[2] says:

"In mitral lesions the left auricle is dilated as a primary consequence of the condition of the circulation; hypertrophy follows, but is insufficient to prevent increased fulness of the pulmonary veins. This impedes the circulation in the lungs, and increased tension in the pulmonary artery soon begets the necessary hypertrophy of the right ventricle."

Bramwell[3] says that—

"Compensation is partly due to hypertrophy and dilatation of the left auricle, but chiefly to secondary hypertrophy of the right ventricle. The systemic venous circulation may for a considerable time be protected by the hypertrophy of the right heart."

Wilks[4] is less clear; but refers to the well-known hypertrophy of the right ventricle, and of the right auricle also, in the pulmonary obstruction of chronic bronchitis, and that in mitral stenosis a similar hypertrophy occurs in the right side of the heart.

Broadbent[5] speaks only of hypertrophy of the right ventricle in connection with the stage of compensation in mitral obstruction.

Bristowe[6] agrees with the American authors referred to in describing the compensatory change as one of hypertrophy and dilatation of the right ventricle.

Stenosis of the mitral orifice is always a very chronic process requiring years for it to contract sufficiently to cause material obstruction, so that the impediment to the pulmonary circulation is very slowly produced. In addition to this the pulmonary circulation is one of very low tension—nearly as low as that of the portal

[1] Practice of Medicine.
[2] Quain's Dictionary of Medicine, vol. i. p. 624.
[3] Diseases of the Heart, p. 181.
[4] Fagge's Principles and Practice of Medicine, 2d ed., vol. i. p. 956.
[5] Harveian Lectures, Brit. Med. Journ., 1885, vol. i.
[6] The Theory and Practice of Medicine, p. 502.

circulation. Lichtheim[1] found that after ligaturing one pulmonary artery the same amount of blood continued to reach the left heart. It was only after about half the lung supplied by the remaining pulmonary artery was rendered bloodless by artificial emboli that the pressure in the aorta began to sink.

In view, then, of the low tension of the pulmonary circulation and the gradual development of the obstruction, the increased resistance offered to the right ventricle will develop so slowly that ample time will always be given the ventricular walls to hypertrophy to meet the increased labor devolving upon them. The only question in doubt is the degree of hypertrophy. This will probably depend chiefly on the general health of the sufferer. If, as frequently happens, he is subject to mild recurrent attacks of rheumatism, each increasing the thickening and contraction of the valves and at the same time maintaining a condition of anæmia and low vitality, the hypertrophy of the right ventricle will be hindered proportionally to the impairment of the health.

The maintenance of the health of these patients becomes, then, a question of the first importance. This, with judicious "training" of the heart muscles by systematic physical exercise, offers the most effective means at our command for prolonging life with the greatest degree of comfort and usefulness, and for warding off the dropsy that often renders the last days of these patients so miserable.

[1] Die Störungen des Lungenkreislaufs, Berlin, 1876; Brit. Med. Journ., 1894. vol. i. p. 515.

COUGH INDUCED BY POSTURE, AS A SYMPTOM NEARLY DIAGNOSTIC OF PHTHISIS.

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Of course, no positive conclusion can be reached in the diagnosis of a case of chest disease without a careful physical examination. But it often happens that the physician is called upon for some suggestion or treatment in the absence of such an examination. Frequently it is impossible to make a manual investigation at the moment advice is sought. The temperature of the room may make it unsafe to expose the chest of the patient; he may be timid, and for the moment object; it may be desirable to reach a provisional conclusion without his knowledge that he is suspected of having a chest disease; or the patient may be absent while his symptoms are discussed. Then it is that every symptom and fact bearing on the case is specially valuable, insomuch that the smallest diagnostic suggestion should never be forgotten nor lost sight of, and it is frequently possible from such considerations to form a tentative judgment of much value as a basis for temporary advice and treatment.

The gradual or rapid onset and the rate of progress of the symptoms; the presence, continuation, and character of fever; whether it is preceded by chill or chilliness, and followed by perspiration of whatever character; the appetite, digestion, and character of intestinal action; the effect of the disease on the general nutrition of the system, as shown by changes in body-weight, and cachexia and other appearances of the skin; the amount of physical strength and endurance; the rate and character of the pulse and respiration, and the sensations attending the latter; pain and discomfort, and their locality and peculiarities; cough and expectoration, and their char-

acter and degree; hemorrhages, their character and frequency, and their relation to fits of coughing; dyspnœa with or without exercise; hoarseness and other changes in laryngeal function; dysphagia; alteration of the finger ends and nails, and many others are all symptoms and signs of great meaning in the diagnosis of chest diseases, especially pulmonary tuberculosis, and may often be relied upon for prognosis and for treatment, even without a critical physical examination. All these considerations have received more or less careful discussion at the hands of students of the subject. The character of the cough as to source, loudness, and quality, was of old regarded as significant, much less so now; and the uniform belief in the necessity and value of free expectoration led to the wholesale use of expectorant medicines; a loose cough was desirable, and a tight, dry one was, of all things, undesirable—doctrines that, in a way, are still sound. The character of the expectoration was always important, but much too large a degree of significance has been thought to attach to the shape and appearance of the sputa.

The causes of cough in substances inhaled and atmospheres encountered have become well understood, but cough induced by posture of the bronchial tubes has received scant attention. Indeed this phenomenon is rarely thought of, and the literature of medicine is almost silent on the subject.

It is probably speaking within strict bounds to say that in more than nine-tenths of all cases of unilateral pulmonary tuberculosis, and of other diseases similarly localized and inducing fluid products, at some time in the course of them cough is to some degree, slight or extreme, produced or aggravated by posture of the patient, and especially by the horizontal posture on the diseased side, when maintained from a few minutes to an hour. Cough is rarely so produced in any other disease whatsoever. In phthisis, especially early in the cases, the cough is increased or produced by recumbency on the side affected, provided the side is only moderately involved and the lesion is somewhat circumscribed in character and situated some distance from the outer surface of the lung. If the disease involves the whole of a lung, the patient often coughs less when he lies on that side.

During the early months of a case, cough may be provoked by

the posture referred to, and later the symptom disappears; then it may appear on the opposite side. Such a sequence is almost certain to be produced in the following manner: The disease at first is localized in one lung (usually about the larger bronchi) and always some distance from the outer surface of the organ; and then any posture that brings the healthy peripheral region inferiorly to the diseased one usually either provokes or aggravates cough. But the disease extends to the lung surface, and all the bronchi and air-vesicles become involved, more or less filled with muco-pus, and insensitive to the presence of it, and cough ceases to be induced by the posture. The patient can lie upon the side involved without discomfort. Then the disease starts in the opposite lung, and the same cough phenomenon is produced by recumbency on that side, and usually the patient dies or passes into a state of nervous apathy before the symptom disappears by the extension of the disease.

Unquestionably the symptom under consideration is produced by the flow of muco-pus into healthy bronchial tubes of lessening diameter, and the force of gravity produces this in most cases where the secretions are fluid, and when the patient lies for any length of time on the affected side.

In the majority of cases of phthisis the lesion at first is circumscribed, and has outside and beneath it a considerable area of healthy lung tissue, the bronchi of which reduce rapidly in diameter from within outward and downward. The slightest entrance of tuberculous matter into these healthy small bronchi, whether brought by posture or by aspiration, usually produces cough in an automatic effort to expel it.

In tubercular phthisis, especially unilateral and apical, its most common form, usually there is more or less thin secretion, muco-pus and serum, in and about the focus of disease, which is easily moved by currents of air and by gravity. Of course it is moved most easily in the direction of enlarging tubes, toward the trachea, but, aided by gravity, the aspirating force of ordinary respiration readily draws it into the smaller bronchi in the opposite direction, where it causes cough, if the mucous membrane of these bronchi has its normal sensitiveness. Recumbency on the affected side favors this result, and so causes cough in a large proportion of cases. If the smaller tubes are not sensitive to the touch of the tuberculous mat-

ter, it produces within them râles, which often annoy the patient and lead him to force a cough to clear them away. Recumbency on the opposite side favors the flow of the secretions toward larger and larger tubes, where the mucous surfaces are less sensitive and more accustomed to such irritations, and the space is abundant for the phlegm to accumulate to a considerable extent along the walls of the tubes without inducing râles or rhonchi. Fluid flowing tracheaward meets few or no obstacles for a long time. The longer it remains and is exposed to the respiration air, the more it is reduced in bulk by drying, and so frequently the patient will harbor in this manner all the accumulations of a night without coughing. The common experience of phthisical patients is to expectorate most in the morning—often they bring up little at any other time. The more or less dried material is started and dislodged with the aid of more fluid mucus developed beneath it. The mucous membrane of the large tubes and trachea, accustomed to the contact of foreign substances in the respired air, is less easily irritated, and so cough is not provoked till relatively large masses of phlegm have accumulated. The finer tubes are more sensitive (or the parts are sensitive to the early production of râles which provoke cough), and so the slightest intrusion of irritating matter into them, so long as they retain their normal irritability, is promptly resented by the most potent act possible, which is cough. This irritability is positively one of the most conservative forces of the economy, for the absence of it allows, or would allow, the air vesicles to be aspirated full of mucus, to the great harm of these cavities and to the function of respiration.

If the secretions at the focus of disease, where they are formed, are very tenacious and sticky, they may flow with such difficulty that they are rarely forced into the smaller tubes by any means; then no cough is produced by position of the patient. In such cases the râles are sibilant and crackling, and suggest thick mucus; and the substance is difficult of expulsion from the tubes and trachea—remaining to undergo more or less decomposition and absorption of products; and little by little to be formed in successively finer tubes as the disease spreads—one of the most hopeless forms of the affection.

Since, then, cough made or increased by the horizontal posture on one side of the body strongly suggests a lesion of the lung in a

certain region of the same side, it is evident that that lesion is nearly certain to be tuberculosis in some form.

Non-tubercular bronchitis is substantially always a bilateral disease, and lateral decubitus does not provoke cough by one side more than the other. Bronchiectasis may be unilateral, but this is a very rare condition anyway, and it is attended by certain symptoms of periodical large evacuations of muco-pus for long periods of time, with little influence on the system in general.

Infarction and foreign-body pneumonia are unilateral, but they are extremely infrequent. Both these conditions may be very confusing from a diagnostic standpoint, even when a physical examination is made, and the former is generally peripheral.

Catarrhal pneumonia is often unilateral, and may be sharply circumscribed, but in adult persons it is rare save as produced by foreign-body irritation, by an infarction or by tuberculosis. When we consider the relative frequency of the diseases named, occurring unilaterally, it is fair to assume that if cough is produced with equal facility in each of them by recumbency on the affected side, then cough thus induced in the sick may be said to indicate tuberculosis on the particular side by more than ninety per cent. of certainty, and by the same reasoning by which we determine that the white sheep eat more than the black ones.

If, then, the phenomenon under discussion has a large measure of diagnostic value, as here contended, it becomes at once a matter of paramount importance to search for and consider it. I am certain that in the cases that cannot be examined physically, it will be found a consideration of the first importance, both as helping to determine the presence of tuberculosis and the location of it.

But in a small proportion of cases, where a critical physical exploration can be made under circumstances the most favorable, it does happen that a tubercular lesion just beginning on some spot of the surface of a large bronchus fails to produce any abnormal sign discoverable by physical examination ; fails to change from the normal the physical capacity of the chest to transmit vibratory impulses—which must always be our main dependence in physical exploration of the chest. In these cases the patients are usually brought for examination because of the cough ; they have rarely become so much reduced in vigor as to arouse suspicion. In not a

few instances of this kind sufficient secretion is produced by the lesion to flow into the distal bronchi when they are dependent, and produce cough or aggravate that already existing, and if we will only faithfully inquire as to this circumstance, we shall find a valuable diagnostic aid in those cases where the patient, or his friends, are sufficiently observant to be trustworthy and accurate witnesses. Unfortunately the physician must mostly rely on the testimony of others as to the phenomenon; he rarely is able to verify it by his own observation, and many people are poor observers of symptoms even in themselves, but a little sharp cross-questioning will often, without leading the patient to his answers, bring him to remember and give valuable symptom evidence about himself.

The following cases illustrate well some of the changes of the posture cough phenomenon in pulmonary tuberculosis; the occurrence of the phenomenon requires no illustration.

It is to be remembered that as long as the disease is restricted laterally to the central portion of a lung, with some normal lung tissue and smaller bronchi situated peripherally to it, so long will any flowing of the muco-pus into the last-named parts cause cough, hence any posture that favors this may induce the symptom. But as the disease progresses peripherally, and successive portions of lung tissue, with their bronchi, become involved, there is less and less normal surface to be irritated, and so there is a lessening tendency to cough from this cause; and when, as occasionally happens, the lung becomes invaded to its very surface, all tendency in this direction ceases, and the patient, who has previously been unable to lie on the affected side without marked increase in the cough, now finds he can do it without the slightest disturbance of this sort.

Miss B., aged twenty-four years, during the early months of 1893, developed a rapidly progressing tuberculosis of the left lung. Rest on her left side in bed produced cough within a few minutes, which continued incessantly, or was often repeated, as long as the posture was maintained. Recumbency on the opposite side was coughless, or nearly so. By the end of the year this tendency was found to be decreasing, and finally it ceased altogether. Then it was discovered that the left lung was involved to its pleural peripheral covering throughout its whole length; it was taking very little air, and was filled more or less with muco-pus which produced crackling râles. I saw her in March and found this condition; she could rest with comfort on the left side. But now, to her surprise, she had just

discovered that decubitus on the right side provoked a little cough, and the examination revealed a slight deposit in the right apex. Another examination in May revealed a marked increase in the lesion in the right apex, and the tendency to cough on lying on that side had steadily increased. Hardly a particle of air entered the left lung, and she could lie on that side with freedom from cough.

Nothing could possibly illustrate better the principle contended for than this case. As long as the disease was confined to the left side and yet had not reached the most distal bronchial regions, cough was produced by every attempt to lie on the affected side, and sleep could only be procured on the opposite side. As soon as the whole bronchial tree was involved, the patient could rest on the left side with impunity. Then when the right apex was attacked, it was found at once that rest could only be obtained on the opposite side.

The following case of very long standing is interesting as proof of the same reasoning :

Miss T., aged fifty-eight, had been a vigorous woman till thirty-five years old. Then she began to have frequent colds, which would often continue for weeks and months. The attacks progressively became extended in duration and less disposed to recover completely. She would expectorate vast quantities of mucus in the attack ; cough was frequent and severe, and for twenty years she could hardly sleep on her left side on account of excessive cough induced by that posture. She has slowly but steadily become worse as the years have passed, and two or three years ago began to notice that left recumbency was less productive of cough ; it steadily decreased till, a year ago, the phenomenon ceased altogether, and she has been able to sleep on that side better than in any other posture. Within the last year she has found that lying on the right side produces cough, and now she cannot assume that position for five minutes without it.

A physical examination of this patient is most interesting. The left chest is distinctly depressed, anteriorly and superiorly, from evident contraction of the lung, which has in some measure uncovered the heart, the sounds of which are distinctly louder than normal. This side measures three-quarters of an inch less than the right, and its movements are distinctly restricted. It is everywhere more or less dull, and its fremitus is increased. Crackling râles are heard over most of it, and the true vesicular murmur is nearly abolished, while there is, especially over the upper portion, tubular breathing, which, over the infra-clavicular region, is distinctly amphoric.

The right side, on the other hand, is remarkably resonant throughout, expands freely, and has nearly perfectly vesicular murmur, except over the upper third, where there are abundant moist râles with some bronchial

breathing, most at the apex. She is unable to say what was the result of previous physical examinations.

The expectoration is mostly mucus, with a small admixture of pus, which contains numerous bacilli of tuberculosis.

There seems to be no reason to doubt that in this case the disease was for many years confined to the left side; that there it gradually extended from the larger bronchi peripherally; that until it reached and involved substantially the whole of the bronchial tree, cough was produced or aggravated by left lateral decubitus; and that the instant this extension was reached the cough phenomenon ceased promptly. Nor is there any evidence that the disease on the right side is of long standing, but every reason to believe that it is of recent date, and that it is wholly responsible for the cough phenomenon of the right recumbency.

GASTRO-ENTERIC RHEUMATISM.

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In his interesting description of nervous dyspepsia marked by an excess of hydrochloric acid in the gastric juice, Mathieu seems inclined (*Traité de Médecine*, vol. iii. p. 270) to ascribe the gastralgic and neuralgic pains of the disease to a local action of the excessive secretion upon the walls of the stomach. He recognizes the intimate relation between this morbid condition and neurotic and arthritic states of the body, but he does not sufficiently emphasize the fact that in many, if not in all such cases, we have to deal with a distinct and definite form of rheumatism that merits recognition and designation as rheumatic dyspepsia. This is just as much a local disorder of the nervous and glandular apparatus of the alimentary canal as rheumatic tonsillitis is a definitely localized manifestation of arthritic disease in the fauces, or as podagra is a local exhibition of gout in the feet. It is, accordingly, among members of the arthritic class of patients that this form of gastralgia and dyspepsia is encountered. It is in advanced life or among prematurely aged and exhausted subjects that this species of rheumatism is most commonly observed. Some of the worst cases occur among middle-aged ecclesiastics and other sedentary people with slender muscles, but with plenty of time and zeal for copulation, which for such persons constitutes the type of neuro-muscular excess. Some of these patients have suffered in earlier life with inflammatory rheumatism; some have had genuine articular gout; sometimes a tendency to obesity is evident; diabetes and polyuria occasionally appear. Premature whitening of the hair, early baldness, erythema, pityriasis, eczema, hemicrania, neuralgia, asthma, chronic bronchitis, lithiasis, various functional disorders of the kidneys, and varicosity

of the hemorrhoidal, scrotal, and peripheral veins are of not infrequent occurrence. Sometimes the same patient exhibits a group of these diseases at once, or he experiences them singly and successively. Sometimes they are distributed among different members of the same family, so that while one is obese another will be diabetic, a third rheumatic, a fourth hemorrhoidal, and so on.

But, with advancing years, the tendency to vague, wandering, neuro-muscular manifestations of the diathetic vice becomes more pronounced and inveterate. The grave disturbance of comfort that is thus produced, and the intolerable mental anxiety that may be caused by failure to recognize the true character of the disorder, give to rheumatic dyspepsia an importance greater than is usually assigned to it in the ordinary text-books and treatises on medicine. Thus, Eichhorst, in his description of diabetes, gives a summary of the symptoms of gastro-enteric rheumatism as sometimes present in the course of the glycosuric disease, but he does not seem to recognize its independent character as a concurrent manifestation of arthritism, and he enumerates its symptoms as a part only of the symptomatology of diabetes.

I desire, therefore, to call attention to this particular form of rheumatism affecting the nerves of the alimentary canal, because it is the cause of a great amount of misinterpreted and, consequently, unrelieved suffering. Its painful paroxysms are experienced when the stomach is nearly or quite empty, several hours after taking food. They are therefore suffered toward noon or in the latter part of the afternoon, or during the night—usually after midnight, though sometimes as early as ten o'clock in the evening, or as late as five o'clock in the morning.

The location of the pain is generally abdominal, usually occupying the epigastrium or the hypochondrium. It is not limited to a single focus, but seems to occupy a considerable territory as if by diffusion ; or, to compare spatial sensations with visible objects, as if it were an ill-defined nebula instead of a luminous star. Sometimes pain is felt in the cardiac region ; occasionally it is more evident in the muscles of the upper arms than in the trunk. The character of the pain is very peculiar, and is of a nature that distinguishes it from other abdominal pains. It may be accompanied by tenderness of the epigastric region, particularly in the sternal

third of the right rectus muscle; but such tenderness is distinct from the paroxysmal pain of gastralgia. Gastric pain is not increased by pressure or by movement. The patient may cough, sneeze, laugh, walk, or run without in any appreciable manner influencing the location or the character or the severity of the pain. Its intensity is not usually very great, though it may be sometimes horribly severe and attended with a feeling of fearful exhaustion. It is a dull, deep-seated, widely diffused, and persistent distress, quite different from the pain of ordinary gastralgia, hepatalgia, renal or intestinal colic, or peritonitis. It must not be confounded with the pains that occur in the gastric crises of tabes dorsalis or in chronic alcoholism, or in peripheral neuritis of any other kind. By the sufferer it is readily distinguished from pains that have their seat in the abdominal walls, and that sometimes occur in paroxysms which alternate with the paroxysms of gastro-enteralgia. In short, the pain of which I speak possesses all the characteristics of neuralgia affecting the ganglionic nervous system rather than the cerebro-spinal nerves of the body. Such pain, when severe, is more intolerable than ordinary peripheral neuralgia.

Rheumatic gastro-enteralgia exhibits a marked tendency to alternation with the neuralgias and myalgias that occur in other nerve territories. In this respect it conforms to the rule that governs the exhibition of vague, wandering, neuro-muscular rheumatism. The patient frequently complains of pain in the face and eyes, to-day; in the neck, throat, and shoulders, or in the heart, to-morrow; the abdominal viscera being next invaded. Sometimes the disturbance affects the cortex of the brain, causing insomnia instead of actual pain. When the gastric plexus of nerves becomes involved, the painful paroxysms are more regularly recurrent than in other parts of the body. In the corresponding enteric plexus it sometimes persists for a long period of time. Of this variety the dyspeptic and arthritic Samuel Pepys, of blessed memory, has left a graphic account in his immortal diary (September 27–October 13, 1663).

When the disturbance is thus shifted to the enteric plexus the distress is usually less severe, but not less annoying, than when it invades the stomach alone. Sometimes the pelvic nerves are the seat of irritation, and the patient may suffer intensely with rectal or vesical agony. Sometimes the sexual organs participate in the

general disorder, and the patient is harassed by prolonged and painful nocturnal erections. Like the analogous priapism sometimes experienced by gouty subjects, this condition soon yields to potassium iodide and to small blisters upon the perineum. In neurotic patients who are liable to pain as the concomitant of weather changes and barometric disturbances, it is not unusual to note an increased frequency of attacks during the damp and changeable weather of the spring and fall of the year. On such occasions, especially after severe fatigue, the gastric paroxysm is frequently accompanied by transient fulgurant pains like those of tabes dorsalis.

During the intervals between the paroxysms, especially if food and sleep have been procured, bodily comfort may be complete. But the close of gastric digestion, or the occurrence of bodily fatigue, or an exposure to cold damp air may be immediately followed by a return of pain. At first, the general health does not appear to be appreciably affected, but after a while loss of sleep, loss of appetite, and persistent mal-assimilation produce a condition of exhaustion. The patient becomes morbidly sensitive to cold; he is neurasthenic and quite incapable of mental or physical activity. Yet some of these sufferers present a florid appearance, and retain their usual weight. As a general rule, however, they gradually become anæmic and cachectic. Many of them are hypochondriacal; and some of the more intelligent class suffer severely through apprehension of malignant disease involving the stomach or other abdominal organs.

The diseases from which gastro-enteric rheumatism must be distinguished are:

Abdominal gout.
Rheumatism of the abdominal muscles.
Subacute peritonitis.
Chronic pancreatitis.
Chronic hepatitis.
Hepatic colic.
Renal colic.
Chronic catarrhal gastritis.
Ulcer of the stomach.
Carcinoma of the stomach and adjacent viscera.

From abdominal gout the disease may be distinguished by the history and habits of the patient.

From rheumatism of the abdominal muscles this disorder is differentiated by the absence of tenderness on movement or manipulation of the muscles. The concurrence of muscular tenderness with gastric pain is not uncommon, and this renders the diagnosis more difficult under such circumstances. It then becomes necessary to note particularly the recurrent incidence of pain, and its association with an empty stomach.

From peritonitis a distinction is established by the absence of fever, tenderness, tympanites, and other symptoms of serous inflammation.

From chronic pancreatitis the disease may be distinguished by the situation and character of the pain, and by its recurrent coincidence with emptiness of the stomach.

The same thing is true of the difference between this gastric disorder and the various painful affections of the liver.

Biliary colic is irregularly recurrent, but it is frequently followed by jaundice and by fecal changes that are absent in gastro-enteric rheumatism. It, moreover, has no relation to the state of repletion of the stomach.

Analogous differences may be noted between the attacks of renal colic and the paroxysms of rheumatic gastralgia.

From the ordinary chronic catarrhal gastritis the disease differs in the greater severity and intermittence of the pain by which it is accompanied. Other symptoms of arthritism can be also discovered; and, if the intestines do not share in the disorder, the nutritive functions are but slightly disturbed.

From ulcer of the stomach the disease differs in the paroxysmal recurrence of pain that is not increased by pressure or aggravated by taking food.

From carcinoma of the stomach it is differentiated by the absence of tumor; by the intermittent character of the pain; by the relief that is obtained on taking food; and by the overabundance of free hydrochloric acid in the gastric juice.

The pathology of the disease still remains as unsatisfactory as that of rheumatism in general. It seems probable that the symptoms are the result of toxic influences affecting the tissues as a con-

sequence of hepatic and renal insufficiency. Just as in strictly gouty cases the agency of uric acid has been demonstrated, and as in uræmia certain definite symptoms exist, so it is more than probable that under certain conditions of retarded oxidation, toxic substances may be generated in the tissues, or taken up from the alimentary canal, and circulated with the fluids of the body to the painful detriment of the sensory apparatus of the nervous system. That the presence of these toxic substances is largely due to hepatic insufficiency is rendered probable by the good effects that follow the use of cholagogue stimulants and a proper regulation of the diet. Much better results generally follow a careful supervision of the alimentary canal and its appendages, than when the kidneys alone are addressed. Great relief from present suffering is obtained through free perspiration, but this measure is more palliative than curative.

Why the local manifestations of disorder are as varied and transient as they are cannot be readily explained. It is probable that the different symptoms that are exhibited by different patients, and the variety of painful sensations that are experienced by the same individual, are due to differences in selective action and degree of saturation on the part of the toxines and the various tissues of the body. It is possible thus to explain the variations that intervene between trifling excitation and complete paralysis of sensation; but the intermittent and erratic character of the attacks is not so easily interpreted. When the seat of disturbance is in the muscular layer of the gastro-intestinal wall, the phenomena of cramp or of paralysis are most conspicuous. If the secretory nerves and the corresponding glands are excited, pyrosis, hyperchloridria, or diarrhœa may be experienced. If, as occasionally happens, the peritoneum be invaded, a most excruciating and dangerous form of peritonitis follows. But if the great network of ganglionic nerve fibres alone be involved, the symptoms of gastro-enteric nervous rheumatism are displayed.

The discovery that when this form of rheumatic pain affects the gastric plexus there is present an excess of free hydrochloric acid in the gastric juice, suggests the thought that here is a condition of the organ analogous to that of an overtaxed muscle that is painful after fatigue. We know that the disintegration of muscular tissue

during work sets free an excess of sarcolactic acid in the muscle. So long as this is retained in the muscular tissue during the partial stagnation that may occur after the cessation of exertion, the muscular nerves are rendered uncomfortable, and the patient complains of a species of soreness in the affected part. But when the excreta of the muscle have been removed by rest, or by massage, or a warm bath, complete relief is experienced. If, however, under such circumstances there be exposure to wet and cold, especially if the patient be arthritically disposed, elimination is not accomplished, and a form of inflammatory departure from the normal standard of nutrition is set up. This, however, does not explain the periodically recurring sensations of pain that are experienced when the stomach is empty. It seems probable that they result from a condition of the gastric mucous membrane that retards the absorption of gastric juice at the close of digestion in the stomach, so that the excess of hydrochloric acid acts upon the nerves of the hollow gastric muscle, in a manner very like what is experienced in the locomotor muscles of the body when fatigue and stagnation follow a period of over-exertion and over-production of sarcolactic acid. It is also more than probable that in the conditions of retarded oxidation and faulty nutrition that characterize the arthritic diathesis, the gastric juice may contain other noxious agents beside an excess of hydrochloric acid.

The urology of these cases must be postponed for the present. Its indications are exceedingly variable and very obscure. The chemistry of the urine in erratic rheumatism is yet to be written.

The treatment of gastro-enteric rheumatism does not differ from that of other varieties of neuro-muscular rheumatism. Like other cases of intense neuralgia, the severest cases of gastralgia and enteralgia require the palliative exhibition of opiates. But, fortunately, the ordinary, the commonplace forms of the disease are more easily relieved. When the period of distress occurs three or four hours after the last meal, it may be promptly arrested, in many cases, by a crust of bread or a glass of milk or a cup of hot water. The patient, however, must be cautioned against reliance upon such measures alone, for they sometimes aid in effecting dilatation of the stomach. I once saw a middle-aged man who had accidentally discovered the palliative quality of milk, and who, consequently, car-

ried in his pocket a quart bottle of milk, from which he drank whenever he felt a pang of pain. This had resulted in an enormous dilatation of the stomach without cure of the disease. Slightly alkaline liquids, such as lime-water, etc., are useful. When the gastric juice contains an extraordinary quantity of hydrochloric acid, it may be necessary to give sodium bicarbonate in scruple doses, three or four times a day. Still better, because more curative, is the sodium salicylate, which should be given in ten-grain doses every three hours until the tissues are saturated with the drug. Salol may be used with advantage if the stomach objects to the salicylate. Both of these preparations are useful also by reason of their active cholagogic property.

Chief among the remedies that are both curative and palliative is olive oil. The patient should take half an ounce or an ounce of salad oil whenever the stomach is empty. This also relieves the constipation that is so commonly present; and by liquefying the bile renders its discharge more easy and certain. In cases of obstinate constipation, it is desirable to employ laxatives that stimulate the excretion of bile:

℞.—Podophyllin. . . . . gr. $\frac{1}{10}$.
Fel. bovin.)
Euonymin.) . . . . . āā gr. j.
Ext. hyoscyam.)
Sig.: Pil. tal. t. i. d. capiat.

The chronic character of the disease renders necessary a resort to alteratives, in many instances. Small doses of mercury (hydrarg. biniodid., gr. $\frac{1}{100}$) three times a day; potassium iodide with colchicum:

℞.—Pot. iodid. . . . . ℥j.
Vin. colchici sem. } . . . . . āā ℥j.
Aq. cinnam. }
Sig.: Gtt. x, t. i. d. capiat.

—together with tonic doses of quinine or of elixir calisayæ, must be administered for many successive months. Sometimes a course of nitric acid, or of the ammoniated tincture of guaiac, is very beneficial. Occasional mercurial purges should not be neglected; and flushing the colon with hot water is often a means of great relief.

The late Mr. Pepys extols the efficacy of large clysters composed of warm ale in which butter and sugar had been dissolved. It is probable that the popularity of hot toddy at bedtime has a similar foundation among old people.

Of great importance is the regulation of the diet. If the patient has been a full feeder, florid in complexion, and inclining to the gouty variety of arthritism, he should be placed for a time on vegetable food, with little or no meat. Mineral waters, of the Vichy and the Carlsbad type, will be found useful in such cases. But this regimen must not be carried too far. Insufficient alimentation will surely aggravate the paroxysmal attacks. One of my clients, who frequented a notorious downtown lunch counter, used to claim that for a fifteen-cent meal at noon he could be sure of gastralgia at five o'clock, while for twenty cents he could purchase perfect immunity during the whole day. Elderly patients who are thin and neurotic often get help from small quantities of brandy or whiskey after meals; but this remedy must not be taken habitually, for in the long run arthritic subjects are very intolerant of alcohol. Debilitated patients who are easily exhausted, and who crave food at short intervals, should have a nitrogenous diet, with very little saccharine and starchy food. Such patients can sometimes eat a hearty dinner, with pickles, cheese, and nuts, without discomfort; but the experiment should not be often repeated. When fats disagree, causing acid eructation, etc., they should be eliminated from the dietary; but when they are digested, they exercise a beneficial influence. It is probable that the good effects of cod-liver oil in many cases of chronic rheumatism may be thus explained.

Frequent warm baths are exceedingly grateful—hence the benefit derived from the various hot springs by people who will not bathe at home. The best result from bathing is obtained from its association with massage. The patient should rise early, take a very light breakfast, then enter the bath, and be thoroughly soaked and manipulated at a temperature of 90° to 95° F. Another light meal may then be eaten, and the patient should remain in bed until noon, the latter part of the day being devoted to exercise in the open air and to general recreation. Alcohol, tobacco, tea, and coffee must be forbidden, for they are not compatible with arthritism, because they retard those processes of oxidation that need acceleration in

every possible way. Great fatigue of mind and body must also be avoided, for there is a notable connection between fatigue and every explosion of rheumatic pain.

DISCUSSION.

Dr. J. H. Musser: I rise to question the propriety of the use of the term gastro-enteric rheumatism. We are all acquainted with the clinical picture presented by Dr. Lyman, of a condition frequently seen, but I think the use of new terms should, as far as possible, be deprecated. It seems to me we should call this the gastro-enteric type of lithiasis or lithæmia. This disorder, as the clinical history shows, is not a local affection of the stomach alone, but is part of a general morbid process in the gouty subject; and the term which indicates this general process, it seems to me, should continue to be used. With the clinical picture presented, and the method of management of such cases, we can all heartily agree with Professor Lyman.

Dr. J. E. Graham: I have listened with a great deal of pleasure to Dr. Lyman's paper describing this peculiar class of cases; and I agree with the last speaker, that we should try to limit the term rheumatism. If the title of rheumatism is applied to the class of cases which Dr. Lyman has described, then we should use a different term for the acute infectious process which we call acute rheumatism. Although the germ of rheumatism has not yet been discovered, I think we are all convinced that it is an acute infectious disease; and if that is the case, then it is an entirely different affection from that described by Dr. Lyman.

Dr. V. C. Vaughan: I have enjoyed this paper very much. I would like to call attention to just one point. We use the word rheumatism to cover a great variety of things, and I have no doubt that there are many pains in the stomach and intestines differing in origin, which would come under Dr. Lyman's description. It seems to me that we ought to make a distinction between these pains when they are caused by a uric acid condition and when they are caused by something else. We can discriminate these classes one from the other, and it seems to me that it would be better to call those cases which are due to a uric acid condition, cases of gout or gouty rheumatism. We were taught a few years ago that uric acid is a product of imperfect oxidation, and if the oxidation went on more completely, urea would be formed. In other words, we were taught that there was a direct relation between uric acid and urea; that the amount of urea excreted in twenty-four hours is the measure of proteid metabolism in the body, and if it were complete all of the nitrogenous material would be

excreted as urea, and if less complete as uric acid. With the light we now have before us we can say from physiological and clinical reasons, that urea and uric acid are in no way concerned one with the other; that uric acid is not a product of imperfect oxidation, the complete product of which would be urea. Uric acid is not increased when urea is diminished, and *vice versa*. We still may believe that urea is a measure of proteid metabolism, but uric acid is the best measure that we have of cell disintegration, and the larger the amount of uric acid we have, the greater the number of nucleated cells undergoing disintegration. Highly nitrogenous food is followed by an increased formation of uric acid, because such diet feeds the cells and they grow more abundantly. The reverse is the case after meals containing an insufficient amount of nitrogenous food and after the administration of quinine and atropine, which diminish the number of polynuclear cells. It seems to me that if we would attempt to make a distinction between the rheumatic condition which is accompanied by the formation of uric acid, which means excessive cell disintegration, and the forms of rheumatism, so called, that are due to wholly different causes, we would better our classification.

Dr. I. T. Dana: Dr. Lyman's paper has greatly interested me, although unfortunately I did not hear all of it. It seems to me that at the present time the term rheumatism represents a pathological conglomerate. I should not be surprised if the time were near at hand when the term rheumatism would be restricted to the ordinary form of articular rheumatism attended with the liability of implication of the heart, and that the terms rheumatic neuralgia, rheumatic dyspepsia, and various other terms which we occasionally make use of in our present imperfect knowledge about the matter, will pass away. It seems to me that we should gain a good deal if we could soon reach the point of limiting the use of the term rheumatism to the articular inflammation, acute and chronic, which has connected with it the liability to carditis and pericarditis, and give to the other forms of disease, which are now grouped together so often under the head of rheumatism, individual and new names.

Dr. H. M. Lyman: I am quite in accord with the remarks made by Dr. Dana as to the complexity of the diseases known as rheumatism. In writing my paper I was greatly puzzled to know what title to give it. The complexus of symptoms I have described, certainly has no more relationship to acute articular rheumatism than arthritis deformans has to the same disease. I believe, as Dr. Dana says, the time will come when we shall recognize the fact that there are different diseases, closely allied in their dependence upon disordered nutrition and characterized by different conditions of the blood and of the excreta of the body. We shall learn to distinguish them from one another by signs and symptoms drawn from observations such as Dr. Vaughan has referred to. I simply wished in this paper to call attention to

the clinical aspects of a complexus of symptoms which are as clearly defined as articular rheumatism, or any of the polymorphous disorders which are now classed under the term rheumatism.

"Lithæmia" has been employed to designate these states, but that is a very objectionable term, because its use commits one to an hypothesis, and it is derived from the term lithic acid, which is now no longer in use in chemistry or medicine.

THE CHEMICAL PRODUCTS OF THE ANAËROBIC PUTREFACTION OF PANCREATIC AND HEPATIC TISSUES, AND THEIR EFFECTS UPON THE TESTS FOR MORPHINE.

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In the Sonzogna trial, at Cremona, Italy, the expert chemists confounded a putrefactive product with morphine. Selmi, who was appointed by the Government to investigate the case, demonstrated that the chemists who had reported the presence of morphine were in error. This substance was not removed from either alkaline or acid solutions with ether, but could be extracted with amylic alcohol. It reduced iodic acid; but in its other reactions, as well as in its physiological properties, it bore no resemblance to morphine. In frogs, it arrested the heart in systole, which is said never to happen in poisoning with morphine. It failed to give both the ferric chloride and the Pellagri tests.

In the same body there was found a substance which was extracted from alkaline solutions with ether, and which gave with hydrochloric acid and a few drops of sulphuric acid, on the application of heat, a reddish residue similar to that obtained by these reagents with codeine, but in its other reactions it did not resemble this alkaloid.

In the examination of the stomach and part of the liver, sent from Lincoln, Nebraska, the writer, following the method of Dragendorf, obtained in the amylic alcohol extract from alkaline solution a residue which gave, with more or less distinctness, all of the principal color-tests for morphine, but failing to obtain crystals which could be identified with those of this alkaloid, the absence of morphine was reported. Afterward it was quite clearly demon-

strated that death in this case had been caused by a blow upon the back of the head with a heavy piece of iron.

The above-mentioned facts induced the writer to undertake some experimental studies upon this point. In this work the author has been greatly aided by one of his students, E. M. Houghton. The results which we have obtained are sufficient to convince us that the identification of morphine in the liver and other organs in cases of suspected poisoning is beset with difficulties not provided for by the methods now generally employed.

Since the substances which vitiate the morphine tests are of bacterial origin, and since bacterial products vary with the conditions under which the germs producing them grow, it is essential that the putrefactive changes which the tissue undergoes before the tests are begun should occur under the conditions, as nearly as possible, which exist in the cadaver. Neglect of this point has undoubtedly been the chief factor in securing the confidence of toxicologists generally in the methods of Dragendorf and Stas-Otto. Many most skilful chemists have carried companion portions of decomposed tissue, one portion with and the other without morphine, through the processes of extraction recommended by Dragendorf, and have obtained satisfactory results, finding that the proper residue responds to the color-tests in the one instance, and fails to do so in the other. Tissues have been thus tested in apparently every stage of putrefaction, and yet the results have been satisfactory and confirmatory of the methods now generally employed. There is one point, however, which has been constantly overlooked. The putrefaction to which the tissues in these experiments are subjected has been aërobic, while that occurring in the dead body is anaërobic; consequently the putrefactive products are not the same in the two cases.

This leads us to state that in all experimental studies of the value of the tests for morphine in decomposing tissue, the decomposition must be allowed to proceed in the absence of oxygen. This is the first point. The second is probably of equal importance, and this concerns the kind of tissue employed. The upper portion of the small intestine (and the adjacent tissue after death) has a bacterial flora peculiar to itself. These tissues are the ones quite universally examined in medico-legal cases, and consist of the small intestine,

the stomach, the liver, the pancreas, the spleen, and, in some instances, the kidneys. Of course, the bacteria present in the small intestines during life may, after death, extend to all the abdominal and thoracic viscera. Since the liver is so generally examined, we decided to ascertain the effects, if any, of the putrefactive products formed in this organ, decomposing under anaërobic conditions, on the tests for morphine carried out according to the scheme of Dragendorf. Recognizing the fact that arsenic is so frequently employed in the form of an embalming fluid, it was thought best to add this to the liver. The experiment is detailed in the following statement:

Five kilogrammes of ox liver, chopped finely and mixed with two grammes of arsenic dissolved in caustic potash, was placed in a large bottle. The bottle was closed with a cork and sealed with paraffin. A glass tube bent at a right angle was inserted in the centre of the cork, while the other end of the tube was connected by means of a short piece of rubber tubing with a Drechsel wash-bottle. The other arm of the wash-bottle was connected with a receiver filled with water. The rubber connecting the large bottle with the wash-bottle was supplied with a clamp. During the first fifteen or twenty days this clamp was left open, and a large amount of gas passed through the wash-bottle and collected in the receiver. After the above-mentioned time, which varies according to temperature, the passage of gas ceases, and the water rises in the receiver, absorbing the collected gas. When this occurred, the bottle containing the tissue and the wash-bottle were disconnected, and the clamp on the rubber tubing was closed. By this time the chopped liver has become sufficiently fluid to absorb the gas as fast as it is formed, and unless the bottles are disconnected the water in the wash-bottle may be drawn back into the large bottle. The fermentation was allowed to continue for thirty days, counting from the beginning. Then the contents of the bottle, decidedly acid in reaction, and giving off a not disagreeable ethereal odor, were poured into a large dish. A considerable portion of the tissue had become fluid by this time.

One kilogramme of this decomposed tissue was placed in each of three evaporating dishes, and these were marked A, B and C. To B 130 milligrammes of morphine sulphate was added, and to C the same amount of morphine together with 0.5 of a gramme each of indol, skatol and phenol. No addition was made to A. These portions were carried through the manipulations recommended by Dragendorf (*Die Gerichtlich-Chemische Ermittelung von Giften*. Dritte Auflage, 1888).

To each 100 c.c. of dilute (1 : 5) sulphuric acid was added. Then 500 c.c. of distilled water was added to each dish, and the dishes were kept at from 40 to 50 C. for eight hours.

Next, each portion was filtered through a falten-filter (No. 572 of Schleicher & Schull). The fluid passed through quickly and formed a clear

brownish filtrate. The filtrates were evaporated at 50 C. to 600 c.c., and four volumes of absolute alcohol were added to each portion. These mixtures were allowed to stand for twelve hours, and in each a brown resinous precipitate formed. After filtration, the alcohol was removed by distillation. A fatty-like residue formed in each flask on the removal of the alcohol, and this was removed by filtration.

The acid solutions were then thoroughly shaken, each with four volumes of petroleum ether. The ethereal layers, when drawn off and evaporated in portions, left very slight residues.

The residues from A and B gave no reactions on the application of the color-tests for morphine mentioned below.

The residue from C showed minute traces of indol with nitric acid alone and with sulphuric acid containing nitric acid.

The acid solutions were next shaken with benzol. The benzol residues gave no response to the morphine tests.

Chloroform was then employed as a solvent. The residues in this case gave none of the reactions.

The acid solutions were now rendered alkaline with ammonium hydrate and shaken successively with petroleum ether, benzol and chloroform. None of the residues from these solvents responded to the morphine tests.

The alkaline solutions having been subjected to the above-mentioned processes of purification, were shaken, each with five volumes of amylic alcohol. The shaking was frequently repeated during the afternoon, and then the mixtures were placed in separators and allowed to stand for eighteen hours. The amylic alcohol extracts evaporated on the water-bath gave the following reactions:

Reagent.	A	B	C
Nitric acid.	All gave a lemon-yellow color.		
Sulphuric acid.	None showed any change.		
Sulphuric with nitric acid.	All gave a lemon-yellow, slowly changing to pink.		
Ferric chloride.	All gave a dirty green.		
Iodic acid.	All promptly reduced the iodic acid.		
Fröhde's reagent.	All gave a blue color without any violet.		
Sulphuric acid and cane sugar.	All became brownish-red, changing to a wine-red.		

Portions of the amylic alcohol extract allowed to evaporate spontaneously showed the same reactions as those given above.

The remaining portions of the amylic alcohol solutions were now shaken with distilled water acidified with sulphuric acid.

After separation, portions of the amylic alcohol were evaporated and subjected to the above-mentioned tests, with negative results in each case. This shows that amylic alcohol does not dissolve from acid solutions the substance or substances interfering with the morphine tests.

The acid aqueous solutions of A, B and C were again rendered alkaline

with ammonium hydrate and shaken with amylic alcohol. The residues from these amylic alcohol extracts were evaporated and subjected to the following tests:

Reagent.	A	B	C
Nitric acid.	All became lemon-yellow.		
Sulphuric acid.	No change in any.		
Sulphuric acid with nitric acid.	All became lemon-yellow.		
Ferric chloride.	All became bluish-green.		
Iodic acid.	All promptly reduced iodic acid.		
Fröhde's reagent.	All became blue with a faint and evanescent purple in B and C.		
Pellagri's test.	All responded promptly.		

The above-mentioned experiment, which has been repeated with no variation in results, convinces us that the tests for morphine by following the scheme of Dragendorf are altogether untrustworthy.

Naturally, the question arises, what is the nature of the substance or substances which give these color-reactions? The answer that these substances consist of indol and its derivatives suggests itself as a possibility. The probabilities in favor of this answer may be briefly stated as follows:

1. The germs which produce indol and its derivatives are native and, so far as we know, constant representatives of the bacterial flora of the upper portion of the small intestines. There are many indol-forming germs, and while some of these may be present in any tissue they are certainly present, in health and in disease, during life and after death, in the small intestines.

2. Indol and its derivatives are products of anaërobic putrefaction, and this accounts for the fact that the reactions which we obtained are not familiar to those toxicologists who have experimented with tissue allowed to putrefy in the presence of oxygen. The apparatus which we used in our experimental work is practically the same as that employed by E. and H. Salkowski (*Zeitschrift f. physiologische Chemie*, B. viii., S. 462) in the preparation of indol. Moreover, in the preparation of indol the same peculiarity in the evolution of gas is observed as in our work.

It was on account of our belief that indol and its derivatives had been in some instances mistaken for morphine that we were led to add these substances to C in our experiment.

We have obtained several samples of indol and skatol, and have compared the reactions obtained with these on the application of the color-tests for morphine.

The samples of indol may be briefly described as follows:

No. 1. Prepared by myself from decomposing pancreas. It is a brown granular substance, and is probably not chemically pure. This fact, however, does not unfit the sample for experiments on the point under consideration, because any impurities which it may contain originated in the decomposing tissue, and may be present in the same substance obtained from like tissue.

No. 2. Obtained from Merck. The order was simply for "indol," without any specification whether it should be synthetic or putrefactive. It is brownish-red in color.

No. 3. Obtained from Schuchardt and ordered as synthetic indol, which it undoubtedly is. This sample is white and in flakes.

No. 4. Obtained from Kahlbaum. Putrefactive indol was ordered, but the label is simply "indol." This sample consists of white flakes.

These samples were submitted to the following tests:

Reagent.	No. 1.	No. 2.	No. 3.	No. 4.	Pure Morphine Sulphate.
Nitric acid.	Bluish-black with violet border.	Reddish-brown.	Reddish-brown.	Reddish-brown.	Brownish-red, passing into lemon-yellow.
Sulphuric acid.	Yellowish-green.	Brown.	Greenish-yellow.	Brownish-red.	Faint yellow.
Sulphuric with nitric acid.	Same as with nitric acid alone.				Brownish-red.
Ferric chloride.	No change at first, but all become greenish-blue.				Blue.
Iodic acid.	No reduction.				Reduced.
Fröhde's reagent.	Reddish, then dark-blue.	Reddish, then greenish-blue.	Reddish, then greenish-blue.	Reddish, then greenish-blue.	Purple, then blue.

Two samples of skatol (No. 1 from Schuchardt and No. 2 from Kahlbaum) were compared with morphine with the following results:

Reagent.	No. 1.	No. 2.	Morphine Sulphate.
Nitric acid.	All became lemon-yellow.		
Sulphuric acid.	All became faintly yellow.		
Sulphuric with nitric acid.	All became more of a red than with nitric acid alone.		
Ferric chloride.	No change.	No change.	Blue.
Fröhde's reagent.	Green to blue.	Green to blue.	Purple to blue
Iodic acid.	All promptly reduced the acid.		

While it would be comparatively easy to distinguish pure morphine from either indol or skatol, it must be admitted, from the results of the experiments already detailed, that the separation of morphine from tissue decomposing in the absence of oxygen, and its identification are, by the methods now generally employed, so uncertain that the conscientious chemist will seek for methods free from these sources of error before he gives positive testimony of the presence of the alkaloid.

I have spoken of indol and its derivatives as being present in the decomposing tissue, and it should be stated that the number of known indol derivatives is by no means small, and how many others there may be which remain unknown no one can tell. Many of these substances give brilliant color-reactions.

Indol was first obtained by Bayer by the reduction of indigo. Later Kühne and Nencki independently obtained indol with skatol by the putrefaction of albuminous substances. There has been some difference of opinion as to the identity of the indol obtained by putrefaction and that which results from the reduction of indigo. According to Baumann neither indol nor skatol originates directly from the proteids, but both arise from the decomposition of a substance soluble in ether containing alcohol. Skatol is methyl indol.

Indoxyl is an easily decomposable substance, which gives some striking color-reactions, among which may be mentioned the production of indigo-blue with ferric chloride in the presence of free hydrochloric acid. Skatol carbonic acid is another product of putrefaction, E. and H. Salkowski having obtained 1.3 grammes from two kilogrammes of moist fibrin after twenty-six days' putrefaction. Among the known color-reactions of this substance Hoppe-Seyler mentions the following:

1. If a dilute solution of this acid (1:1000) be treated with a few drops of pure hydrochloric acid of 1.2 specific gravity, and then with a few drops of potassium nitrite solution (2 per cent.), a cherry-red coloration is produced, and later a red precipitate falls.

2. If such a solution be mixed with an equal volume of hydrochloric acid and then a few drops of chloride of lime solution ($\frac{1}{2}$ per cent.) be added, a purple-red color is produced.

3. Treated with a few drops of hydrochloric acid, then with two or three drops of very dilute solution of ferric chloride, and heated, the mixture becomes intensely violet before boiling.

Skatol carbonic acid is non-volatile.

Skatol acetic acid has been obtained by Nencki by the anaërobic putrefaction of serum-albumin. The aqueous solutions of this substance give with ferric chloride a white cloudiness which on warming becomes brick-red, and in more concentrated solution fire-red.

Both indirubin and indigo-blue may be formed by the oxidation of indol.

Knowing that indol and its derivatives are formed in anaërobic putrefaction, and that in Dragendorf's scheme for the separation and identification of vegetable alkaloids these substances appear in the residues which are tested for morphine, and knowing the great number and variety of color-reactions given by these substances, it may be asked, how much reliance can be placed on the color-tests for morphine?

Besides the indol bodies certain other substances are formed in the anaërobic putrefaction of proteid substances. Among these are certain aromatic products of the putrefaction of tyrosine. The following may be mentioned:

1. Hydroparacumaric acid (para-oxyphenyl-propionic acid).

This substance gives with ferric chloride a distinct but evanescent blue coloration.

2. Para-oxyphenyl-acetic acid.

This substance gives with ferric chloride a pale, grayish-violet, which soon changes to a dirty-green color.

Among other products of the anaërobic putrefaction of proteids, phenol and parakresol may be mentioned.

Phenol gives with ferric chloride a violet color.

Parakresol gives with ferric chloride a blue coloration.

With the above-mentioned substances in a decomposing liver, and knowing that some of them at least are present in the amylic alcohol residue following the process of Dragendorf, how much reliance, may again be asked, can be placed on the color-reactions of morphine?

Besides the above-mentioned substances, which may be present in decomposing tissue, Mr. Houghton and I have found a crystalline, non-poisonous substance which gives a lemon-yellow with nitric acid and promptly reduces iodic acid. A further study of this body is desirable.

TETANY IN AMERICA.

With a Report of Five Cases.

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Although frequent enough in many parts of Europe, tetany is of sufficiently rare occurrence in this country to warrant the report of the following instances, and to render interesting a review of the cases published in America.

Considerable confusion exists regarding the exact application of the term "tetany." Certain writers would confine it to those cases in which there is a very marked intermission in the spasm, reserving the word "arthrogryposis" for those in which the contraction is more continuous. The condition described as "carpo-pedal spasms" is by some writers considered quite distinct from tetany, and by others, as, for instance, Fagge, viewed as a minor form of it. Strümpell denies the existence of tetany in early childhood, and Henoch draws the line sharply between the disease as seen in children and in adults. Others, as Schlesinger, speak of tetany and a pseudo-tetany, making the distinction largely on etiological grounds. Some would exclude all cases which do not exhibit marked increase of the mechanical and electrical excitability of the nerves and muscles, while others, admitting the great frequency of these conditions, do not consider them as essential to diagnosis.

Finally, several distinct varieties of tetany have been described —as, for instance, rheumatic tetany, chronic tetany, tetany following thyroidectomy, and tetany due to dilatation of the stomach.

The more one studies the subject the more impossible does it seem to establish any line of demarcation between the different

forms of the disease. There are numberless gradations between the conditions of well-marked, widespread, intermittent contractions, and of the continuous or intermittent carpo-pedal spasms. Then, too, some cases exhibit intermittent contractions at one time and continuous at another, or intermittent in one part of the body and continuous in another part. Not every case shows all the cardinal symptoms, including those described by Trousseau, Chvostek, and Erb. While, therefore, it is very possible that two or more diverse conditions may be included in the term, in the present state of our knowledge it seems best to define tetany as a disease consisting of tonic spasms either continuous or paroxysmal; usually symmetrical; affecting especially the extremities, but often widespread or sometimes confined to one limb; not accompanied by unconsciousness, and not depending upon any irritative lesion of the brain, cord, or nerves, or upon hysteria.

Tetany has been so thoroughly described in other countries during recent years that any account of its symptoms would be out of place before this body, and I may now simply present the clinical histories of the cases which I have seen. I regret that the details are in some particulars far from complete.

Case I.—Willie McG., aged nineteen months; fairly well nourished; had several eclamptic convulsions when about two weeks of age; pneumonia at about one year. No note made of the existence of rickets or other form of ill health. About March 17, 1886, he began to vomit and continued this until the 21st. On the 20th he commenced to scream and his eyes turned up and often crossed. The thumbs became flexed into the palms; the fingers firmly bent at the metacarpo-phalangeal articulations, but straight elsewhere and adducted; the wrists flexed; the feet and toes extended. The hands and feet had a somewhat blue and swollen appearance. By the next day all spasm was gone, but by the afternoon of the 23d (two days later) all the symptoms had returned. The abdomen was swollen and tender. During the night following there was some stridulous breathing after cough, and on the 24th the spasm of the extremities was still present although the eyes were now unaffected. Effort made forcibly to overcome the contraction caused screaming. The bowels were constipated; the tonsils enlarged, and they and the pharynx somewhat red; some mucous râles were audible in the chest. The record made on April 1st, one week later, states that the contractions were still present to some extent. The child let the hands hang most of the time with the wrists flexed, and he could not seize a pencil at all easily. He would crawl on his hands and knees instead of on his hands and feet as was his custom when well. On April 14th it was recorded

that full power had returned. About April 21st he developed rubella, which was preceded and accompanied by severe diarrhœa. April 22d, he awoke screaming, the contractions having suddenly returned in full force. The screaming lasted only a short time, but efforts forcibly to straighten the limbs brought it on again. In about three hours the spasm passed away. There was no further trouble until June 14th, when vomiting and diarrhœa with cough set in and continued, and on the morning of the 18th, crying with flexion of the thumbs and wrists and extreme extension of the toes developed. The child kept putting his hands to his feet as though the latter were the seat of pain. He was better in the afternoon, worse at night, and on the next day much as when first seen, except that the fingers were straight and separated from each other. There was no pain except on passive motion. Nothing further was heard of the patient for some years, when I learned that there had been attacks of tetany on several occasions. About three years ago he died of some obscure meningeal affection in the Children's Hospital of Philadelphia. No autopsy could be obtained.

This case illustrates well the close etiological association of tetany with gastro-intestinal disturbance. Pain, it will be noticed, occurred only when the attacks began or when the parts were handled. The stridulous respiration heard on one occasion indicated a tendency to laryngismus, the close connection of which with tetany is so well understood. The separation of the fingers seen in the attack in June is worthy of remark, as it differed from the accoucheur's position more commonly witnessed. For the most part the contractions in this case lasted several days or a week or more, and should therefore be called continuous. On other occasions they were of short duration, lasting but a few hours or a day, and cannot be placed in this category.

Case II.—Charles S., light mulatto, aged two years, was brought to the out-patient department of the Children's Hospital, May 1, 1889. The mother stated that for five months he had had difficulty in swallowing, solid food being taken more easily than liquid. The latter made him choke so that he grew "black in the face" and had to be beaten on the back to make him breathe again. He had also at times difficulty in breathing, the inspiration having a distinctly crowing character. The mother further stated that he sometimes had "spasms" in which the fingers were drawn inward and the wrists flexed, and that this condition would last for "some time." Examination of the child showed him to be a well-marked case of rickets. While in the clinic room his respiration was distinctly noisy, but the clinical notes indicate that it was rather the expiration than the inspiration. This may have been an error. He was ordered cod-liver oil and rock-salt baths, but he did not return. Several futile attempts were later made to see him

in order to study his symptoms more fully. About a year later I learned that he had continued to have the attacks of tetany at intervals.

The brief and incomplete notes of this case serve at least to illustrate the close connection between rickets, laryngismus stridulus, and tetany. The nature of the difficulty in swallowing is not clear. Very probably there was a spasm of the muscles of deglutition accompanied by a spasm of the larynx.

Case III.—Peter W., aged forty-eight years, a well-developed and muscular negro, was brought by the police patrol to St. Agnes Hospital, July 15, 1890, the attack having come on him suddenly while at work. His family history was good, with the exception of the death of his mother from phthisis. He had had "typhoid pneumonia" nine years previously, and had had the ordinary diseases of childhood. He stated that ever since birth he had suffered from "cramps" about once a year, but that for the last few years they had occurred more frequently. He had an attack in the autumn of 1889, another in May, 1890, and a third two weeks before coming to the hospital. They consisted of muscular cramps which were sometimes very painful, and which usually began in the hands or feet and extended throughout the body. The feet would be drawn into dorsal flexion, the knees and hips extended and stiff, the thumbs bent into the palms and the fingers closed tightly over them, the wrists flexed, the elbows flexed and drawn to the sides, and the head held stiff. The jaws would be tightly closed, or sometimes could be opened and not shut again. The breathing would be painful and difficult, and the man feel as though each moment would be his last. The attack would come on slowly and increase in severity. At its height the spasms would be somewhat remittent, lasting some minutes, and then partially relaxing, while the greatest intensity of the pain shifted from one part of the body to another. The whole duration of an attack would be four or five hours.

When admitted he was in great pain and bathed in profuse perspiration. He had a temperature of 97° F., and a full and strong pulse. He was unable to pass water. The spasm and pain made walking impossible. The muscles of the neck, back, and extremities were involved, but particularly those of the latter. The neck was stiff, and there was occasionally slight arching of the back, the weight resting mainly on the shoulders and the nates. The muscles of the calves were as hard as iron, and the pectorals stood out like eggs under the skin. The individual paroxysms lasted one or two minutes, and were followed by complete relaxation, lasting five or ten minutes. An exceedingly anxious expression of face accompanied the onset of the convulsions, which the man dreaded greatly. The spasm never seemed to be present with equal severity everywhere at once, but showed its greatest intensity now in one portion of the body and now in another. The upper extremities, however, were much more frequently attacked. A curious

feature of the case was the fact that if the forearm or leg happened to be in the position of extension at the time of the onset of a spasm, the member stiffened in that position; and the converse was true if it was in flexion. There was no affection of speech. The patient appeared able to open the mouth and move the tongue readily. Percussion of the pectoral muscles during the intermissions produced a momentary vigorous contraction. There was marked anæsthesia of the lower portion of the body as far upward as the umbilicus, the man being unable to feel the prick of a pin.

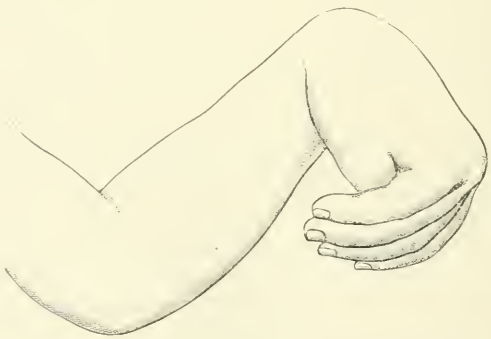
The spasms diminished in intensity in the course of a couple of hours, after hypodermic injections of morphine and atropine had been administered; but they returned later in the day, and appeared even through the next day, the 16th, although with less severity and frequency. On the 17th he felt sore all over and the muscles were tender, but there was no more spasm. Nothing abnormal was found on physical examination of the chest and abdomen. The thyroid gland was unaltered. On the 19th it was observed that compression of the upper arm produced a cramp-like pain in the forearm and a flexion of the wrist. This was relieved when the pressure was removed and friction of the muscles employed. The abdominal, cremasteric, and plantar reflexes were normal. The knee-jerk was absent, even with reinforcement. Efforts to induce ankle clonus produced slight cramp in the calf muscles. Pressure over the exit of the facial nerve was followed by slight twitching of the muscles of the face.

The man had no more trouble while under observation. On the 23d, eight days after admission, it was noticed that there was no longer any anæsthesia of the lower extremities. The knee-jerk was still absent. The course of the attack had been afebrile. About a week after his entrance into the hospital, Dr. G. Betton Massey kindly tested his electrical reactions for me. There was found distinct quantitative increase of the general electrical excitability of the muscles. This was not more marked in any one muscle than in others. No qualitative changes were discovered and the normal formula was invariably present. There was "a decided increase in the electro-muscular sensation, a gentle contraction causing a pain that resembled that of the tetanic attacks."

This instance of tetany is the only one of my cases occuring in an adult, and even here the disease began very early in life. The case is of interest on account of the severity and the wide extent of the spasms. The contraction caused by tapping the pectorals is an instance of the mechanical irritability common in this disease, as is the well-known facialis symptom of Chvostek, also present in this case. Trousseau's symptom—the production of spasm by pressure upon the artery or nerve, especially of the arm—and the increased electrical excitability—Erb's symptom—

were also witnessed. Inability to urinate, from which the man at first suffered, and anæsthesia have been recorded by others also as occurring in this disease. The closing of the fingers over the thumb is not so common as the extension at the metacarpo-phalangeal joints.

Case IV.—Emily W., aged three and one-half years. She was stated to have had good health until the occurrence of severe diphtheria four months before. As she was convalescing palsy set in, involving principally the muscles of the pharynx and lower extremities. Nearly fatal heart-failure is said to have occurred on several occasions. There was no history of the existence of any pain. She recovered very slowly from this condition, and by the end of twelve or fourteen weeks from the onset of the diphtheria she could walk only a few steps. Soon after this she was taken while in church with a severe attack of fainting and had to be carried home. In the afternoon of the same day fever developed and continued during three days. Then, for three days she suffered constantly with great pain, especially when handled. She seemed unable to get into any comfortable position. The pain then suddenly and entirely ceased and simultaneously the hands passed into the bent position, which was, it is said, as marked at the beginning as when I first saw her. Pain did not recur except on passive motion. This condition persisted without intermission for three weeks, during which she was kept in bed; and she was then placed in the wards of the Children's Hospital, October 11, 1892.



On examination, she was found to be a well-developed though decidedly irritable and somewhat delicate-looking child. There was no evidence of rickets. She sat in apparent comfort in bed. The hands were flexed at the wrist to quite a right angle, as shown in the illustration, and the skin over the joint was tense, red, and somewhat œdematous. The fingers were flexed at the metacarpo-phalangeal articulations, but extended elsewhere.

They were also decidedly adducted toward each other, the middle and ring fingers overlapping the others to some extent. The thumb was flexed into the palm, but its terminal phalanx was in extension and protruded between the middle and ring fingers. The feet were extended; the effort to flex them seemed to give pain, but the irritability of the child rendered it difficult to determine how much actual suffering was produced. It was clear, however, that the manipulation of the hands was very painful. The knee-jerks were absent. Rest in bed and bromide of potash were ordered for about a week, but without benefit, and iodide of potash was equally useless.

No change could be observed in the condition for some weeks. Even during sleep the contraction continued, and attempts made to overcome it roused the child with the pain. The patient's irritability and the constant contraction at the wrist prevented at this time any successful attempt to bring on a spasm by compression of the upper arm. Tapping or stroking the face in front of the ear was not followed by muscular contraction. On several occasions the endeavor was made to determine the electrical reactions, but without success, owing to the fear and crying which resulted.

On November 2d, six weeks after the onset of the attack, the child permitted the extension of her hands to a considerable degree and without complaint, if her attention were diverted. She kept them, however, when at rest, in the same position as at first, and was as little able to use them. Persistent careful efforts were now daily made to straighten the hands by manipulation and by placing large balls of raw cotton in the palms. By November 8th there was decided lessening of the spasm, perhaps the result of great improvement in the general health. By November 14th, eight weeks after the onset, the hands were almost entirly relaxed, and, although the thumbs were still in the palms, the child could handle a doll awkwardly. On this date firm compression of the upper arm caused complaint of pain and a slight increase in the flexion of the hand. The feet were no longer extended.

She now improved rapidly, and by December 1st was practically well. When she first recommenced walking, on November 20th, she complained of pain in the feet and cried when they were handled. Later, she developed at different times measles, pertussis, and severe ulcerous stomatitis, but without the return of the tetany, and on May 15th she was in excellent condition, hearty, and well-nourished.

This case is in some respects an interesting one. The position of the wrists in constant flexion, combined with the history of former paralysis, suggested the possibility of a wrist-drop resulting from the diphtheria. A brief study of the patient, however, showed that there was positive contracture. Other interesting features were the sudden cessation of a three days' severe pain

simultaneously with the development of extreme contraction; the persistent absence of the facialis symptom and of any discoverable cause for the tetany other than the diphtheria weeks before. The presence of œdema of the articulations is a common feature where the flexion is persistent.

Case V.—Emma S., six weeks old, was brought to the Children's Clinic of the Hospital of the University of Pennsylvania on December 6, 1892. She had been fed at the breast and was fairly well nourished. She had had no illness, except occasional colic and eructation of gas, and she had not been fretful. Two weeks previously the mother had noticed that the child cried whenever picked up or when its legs were moved, and that its knees were constantly held flexed. She stated that this condition had persisted without intermission, and that the effort to straighten the joints caused crying.

The examination made on December 6th showed that the knees were partially but not rigidly flexed, and that efforts to extend them were painful and caused the hamstring tendons to stand out as hard cords, and the tissues over the knee-caps to appear baggy and wrinkled—apparently the result of stretching by the constant flexion. The knee-jerks were normal. Further physical examination revealed nothing out of the way. The child was ordered bromide of potash and antipyrine, with inunctions of warm oil over the tense tendons. By December 13th, one week later, the legs could be extended more easily and with less pain. Former treatment was replaced by a cough mixture, which a slight bronchitis demanded. By December 19th the legs were decidedly better and the child could herself extend them to a considerable degree. By December 28th, three weeks from the first visit, the legs were still improving, but the baby was losing weight. It had been suffering for a week from diarrhœa, vomiting, and colic, and the mother's milk was rapidly growing so thin and insufficient that artificial feeding was deemed necessary. After this date the legs continued to improve; the gastro-enteric symptoms became temporarily better, but soon returned with increased force. On or before January 11th—*i. e.*, about a month after the first visit—the legs were completely relaxed; but on this date the arms became rigidly flexed at the elbows, the wrists slightly bent, and the thumbs drawn into the palms. When seen two days later, the condition was a little better: the flexion of the left elbow had ceased, the fingers were freely movable, but the thumb was still incurved. On the right side the elbow was still bent, the wrist not so much; the fingers overlapped each other and were strongly flexed over the thumb. Efforts to straighten the right arm caused pain. Compression of the left arm was not followed by contraction, and neither pressure over the exit of the facial nerve nor stroking with the finger in front of the ear had any effect. The knees were still free from spasm.

There was severe bronchitis in addition to the vomiting. Electrical examination made about this date by Dr. Evans, of the Clinic of Nervous Diseases of the University of Pennsylvania, showed a quantitative diminution of both faradic and galvanic contractility, but no alteration of the formula.

For two months from this time, *i. e.*, until the middle of March, the child lost ground steadily in health and became greatly emaciated, although vomiting occurred only occasionally and there was no diarrhœa. A flat, papular, widely diffused syphiloderm had made its appearance. The tetany had returned in the left arm and the elbows of both sides remained always more or less flexed, the thumbs always bent in and the fingers generally clasped over them, and only movable with considerable force. The wrists were not flexed and the knees were only occasionally bent. The feet had assumed the position of marked dorsal flexion, and retained this much of the time. Efforts to straighten the arms always caused pain. After the middle of March, the child's general health began to improve rapidly and the tetany grew much less evident. By March 27th, three and a half months after the first visit, it had gained much in nutrition and weight, although still a miserable specimen. The eruption had spread. The elbows were still slightly flexed; the thumbs were constantly in the palms, and the child cried when they were forcibly withdrawn. There was no spasm elsewhere. Trousseau's and the facialis symptoms could not be obtained.

Up to May 1st the baby had continued to improve, and the contractures by this date were entirely gone except in the thumbs, which were still always fixed into the palms, although not so firmly as before. The eruption was disappearing under the influence of mercurial inunctions. Soon after this a change in the food brought on a return of vomiting, together with a reappearance of the contractures in both elbows. The weather was now hot, and the patient became exhausted, although vomiting had ceased. It died on May 24th, six months after the onset of the tetany. There was no autopsy.

This case is peculiar in several respects. The contracture starting at the knee-joint and persisting there for weeks without involving other parts is certainly an unusual mode of onset. The suspicion was at first aroused that the condition was one of congenital contraction of the tendons: but the later development of contractures at the wrists and elbows, apparently consecutive to gastro-enteric disturbance, made the diagnosis of tetany reasonably sure. Possibly the quantitative diminution of the electrical excitability may have been due to the great muscular wasting. The case is, for the most part, an instance of continuous spasm. The flexion of the wrists lasted scarcely two days and may be called intermittent. The contraction at the elbows was continuous,

although with decided remissions and exacerbations. The contraction at the knees was continuous until they gradually assumed the normal position, after which it became distinctly intermittent. The flexion of the thumbs was obstinately continuous for at least four months.

One is surprised at the paucity of records of tetany to be found in the medical literature of America. I have made a somewhat extended search for cases, both under the heading of tetany and under those of trismus, laryngismus, spasm, and so on, lest some instances of the first-mentioned disorder should be concealed under the names of the others. Undoubtedly numerous cases have occurred which have not been recognized by physicians, and still more, although recognized, have never been published. Undoubtedly, too, I have overlooked the reports of many. Still, the results of the search prove that tetany is undoubtedly comparatively rare in this hemisphere.

For reasons already indicated I have included cases of so-called carpo-pedal spasm, except such as were clearly the immediate prodromal evidences of eclampsia and certainly attended by unconsciousness; for the study even of the few American cases shows that it is impossible to regard carpo-pedal spasm as other than a mild exhibition of tetany.

The following are brief abstracts of the 72 cases which I have been able to collect; arranged, as far as possible, in chronological order—at least as far as the year of publication is concerned. It has been found impossible in these abstracts to make a sharp distinction between "continuous" and "intermittent" contractions. For the sake of convenience I have rather arbitrarily denominated those spasms as continuous which appear to have lasted uninterruptedly for more than two days, and those as intermittent which did not last longer than two days without permanent or temporary disappearance.

The Roman numerals are employed to designate the cases reported with more or less detail. The capital letters, in parenthesis, indicate the brief references without description which have been made to cases other than these.

I. 1833. Eberle (*Diseases and Physical Education of Children*, 1833, 527).—Healthy child of nine months. Repeated attacks of laryngismus. "Spasmodic affection of the respiratory muscles" and opisthotonos lasting ten to twelve minutes. Feet and hands in typical continuous contraction.

II. 1844. A. F. Axson (*New Orleans Med. Journ.*, 1844, i. 45).—Girl, four months. Dentition thought to be cause. Attacks of laryngismus, sometimes with retraction of head; flexion of thumbs into palms; flexion of toes. Spasms last one-half to two minutes; occur often in day. Treated by cold to head.

III. to VI. 1844. J. P. Epperson (*West. Journ. of Med. and Surg.*, 1844, 2d S., ii. 25).—Four children in one family; colored; all under one year. Frequent attacks of laryngismus, lasting few seconds or minutes; later with strabismus, continuous characteristic spasm of feet and hands, and occasionally slight spasm of arms and legs. Treated successfully with stramonium.

(A.) Three other children in this family had earlier died from same condition.

VII. 1848. J. F. Meigs (*Diseases of Children*, 1st ed., 1848, 424).—Boy, seven months. Chronic intestinal derangement. Continuous spasm of hands and feet, with swelling, lasting four months. Occasional spasmodic movements of face, arms, and body. Laryngismus frequent.

VIII. 1848. J. F. Meigs (*Ibid.*, 429).—Child, two years. Attack of tonic flexion of toes lasting a few hours; relieved by purgative.

IX. 1850. C. D. Meigs (*Diseases of Children*, 1850, p. 167).—Boy, six months. Frequent attacks of laryngismus simultaneously with intermittent contractions of hands and feet, opisthotonos, turning of head to right, general rigidity, and finally with development of general convulsions. Death in couple of weeks or less.

X. 1853. J. F. Meigs (*Diseases of Children*, 1853, 2d ed., 463).—Child, nine months. Delicate; persistent digestive disturbance; open wound. General convulsions followed in few days by painful tonic characteristic spasms of hands and feet, nearly continuous for two months, with occasional remissions. Occasional tonic, chiefly intermittent, spasm of arms and thighs, and retraction of head and trunk. Later a relapse with laryngismus.

(B.) In a later edition Meigs and Pepper (*Diseases of Children*, 1870, 4th ed., 529) refer to "two other cases" in which the contraction was decided, but lasted a short time only. One of these is possibly Case VIII., detailed above.

XI. 1858. W. J. Kincaid (*Transac. Ohio State Med. Soc.*, 1858, xiii. 69).—Boy, four and half months. For weeks had had laryngismus badly; then also began to have hands and feet spasmodically flexed in some of severer attacks. Cured by cannabis and chloroform internally.

XII. 1859. R. R. McMeens (*Cincin. Lancet and Observ.*, 1859, ii. 457).—Boy, twelve months. Well developed. Dentition and digestive disturbances considered the cause. Subject to laryngismus. Developed in addition characteristic [continuous?] spasm of hands and feet, with persistent flexion and partial paralysis of upper and lower extremities. Recovered.

XIII. 1862. V. J. Fourgeaud (*Pacific Med. and Surg. Journ.*, 1862, v. 303).—Girl of nineteen months. No cause discoverable except general weakness and emaciation. Nearly persistent tonic spasm of lower half of body; momentary partial relaxations. No evidence of pain. Spasm present during sleep. Spasm gradually became intermittent. Whole duration about six weeks. Disease at first simulated a spinal spastic palsy, as legs were crossed.

XIV. 1866. L. H. Carpio (*Gac. Méd. de México*, 1866, ii. 222).—Blacksmith, fifty years old. Superficial wound of abdomen, and few hours later abundant sweating; slight trismus of left side with powerful painful contractions of left side of neck; paroxysms intermittent; induced by moving head or coughing. Entire relaxation and no pain between paroxysms. attacks ceased in five days.

XV. 1871. Arnold (*Balt. Med. Journ. and Bull.*, 1871, ii. 347).—Nursing woman of thirty-two years. [Appears to have been intermittent] tetany of left side of face, right arm, and slightly of right leg. Sometimes pain in nape of neck. Trousseau's sign present. [Report very incomplete.]

XVI. 1871 Zuñiga (*Gac. Méd. de México*, 1871, vi. 377).—Blacksmith, twenty years. Old suppurating wound. Exhibited trismus, tetanic physiognomy, copious sweating, spasm of muscles, of abdomen, neck, trunk, and lower limbs. Difficult respiration [spasm of intercostal muscles?]. Trismus chiefly persistent. Other contractions more intermittent. Condition had lasted twenty-four days when reported, although improving under chloral.

(C.) Zuñiga (*Ibid.*) says that another case of tetany had been in the hospital a few days before.

XVII. 1872. W. R. Nichols (*Canada Med. Journ.*, 1872, viii. 161).—Boy, sixteen years. Gradual onset; no cause given. Trismus, contortion of face, spasm of muscles of neck and back [opisthotonos], abdomen, and limbs. [No notes regarding hands and feet.] Pupils dilated and oscillating; strabismus; difficulty in swallowing. Spasm continuous, with remissions only. Excitement made worse; no cramp-like pain. Trousseau's symptom present. Recovered after three weeks' treatment with iodide of potash followed by bromide of potash.

XVIII. 1875. M. Alfaro (*An. Asoc. Larry, México*, 1875, i. 97).—Healthy man, thirty years. Slight faintness and tingling in lower limbs ushered in general tetanic rigidity with trismus, distorted features, contracted pupils, adduction of thumbs, extension of feet, legs, thighs, and arms. Respiration interfered with. Four attacks in a few hours, each lasting ten to fifteen minutes. Similar attacks since age of fifteen; first shortly after death of mother; others usually after psychic disturbance.

XIX. 1876. J. S. Green (*Transac. N. Y. Obstet. Soc.*, 1876–78, i. 160).—Delicate girl, four years old. After an attack of diarrhœa there developed intermittent spasms of feet, legs, hands, and forearms, lasting two to five minutes, with some degree of persistence between them. In one paroxysm there was opisthotonos. Position of hands characteristic. Paroxysms so painful that anæsthesia with chloroform required for six hours. Disease lasted in all about forty-eight hours.

XX. 1877. N. B. Emerson (*Transac. Amer. Neurolog. Assoc.*, 1877, ii. 179).—Girl, twelve years. After suppression of first menstruation pain in right arm and leg, followed by continuous contraction lasting a few days. Hands and feet in characteristic position. Then similar attack of left side, preceded by numbness and tingling. Salicylic acid followed by recovery. [As a result?]

XXI. 1877. N. B. Emerson (*Ibid.*).—Male, eighteen years; delicate. Disease began at age of four years, possibly then associated with some affection of brain or cord. Painful spasm, sometimes one arm, sometimes whole body; oftenest arm and leg of one side. Contraction continuous night and day and characteristic; lasted usually two to three days up to ten days. Respiration sometimes difficult. Attack generally preceded by numbness and evidences of indigestion. Trousseau's symptom not obtained: perhaps result of chloral given. Recovery under use of conium.

XXII. 1879. S. Weir Mitchell (*New York Med. Record*, 1876, xv. 604).—This and the following case seem very probably anomalous instances of tetany. The writer gives them no name, but describes them as due to obscure functional conditions.

Boy, seventeen years; fair health. Forty-eight hours after exposure to intense heat had dull pain in the legs, followed next day by great, continuous rigidity of legs. Passive motion caused pain. Recovery in three weeks.

XXIII. 1879. S. Weir Mitchell (*Ibid.*).—Man, forty-three years; well developed. Pain in back and legs, with increasing stiffness, followed in a few hours by fully developed attack. Legs extended, moderately stiff; but least handling caused severe, intensely painful spasms of legs, feet, and abdominal muscles. Recovery in sixteen hours under narcotics. Two previous similar attacks.

XXIV. 1879. C. K. Mills (*New York Med. Rec.*, 1879, xvi. 218).—Girl, thirteen years. Rheumatism, and later diarrhœa. Painful continuous spasm of extremities; elbows flexed; wrists flexed and abducted; thighs and feet extended. Handling left parts painful; knee-jerks increased. Recovered in two weeks, with cure of diarrhœa, by silver and opium.

XXV. 1879. H. P. V. Petershausen (*Detroit Lancet*, 1879–80, iii. 248).—Man, twenty-eight years; healthy; history of blow on head, possibly connected with the tetany. Disease had lasted six years. At one time there had been a very persistent hemiplegic condition, which finally disappeared. When seen, intermittent paroxysms of left arm and hand, neck, and facial muscles every three or four minutes, lasting thirty to one hundred seconds. [Not clear whether legs involved.] Some œdema of hands and face. Attacks preceded by stiffness and pain. Some paralysis of left arm and difficulty of speech during paroxysms and intermissions. Recovery in four weeks under chloral.

XXVI. 1880. A. H. Sowers (*Proc. Nebraska Med. Soc.*, 1877–80, 186).—Adult male; subject to severe dyspepsia; had a fall and suffered some shock, and a few days later tetany devel-

oped. Intermittent spasm of whole right side, with slow respiration. Pain in head and staring expression ; disposition to sleep. Disease had lasted three months.

XXVII. 1882. J. O. Hirschfelder (*Pacific Med. and Surg. Journ.*, 1881-82, xiv. 385).—Adult male ; fall in elevator five days before first attack. Symptoms not detailed, but Hirschfelder showed to his class that pressure on axillary nerve produced general rigidity, retraction of head, and well-marked tetanic convulsions ; relieved when pressure was removed.

XXVIII. 1884. I. W. Smith (*Amer. Journ. Obstet.*, 1884, xvii. 438).—[Case reported under title "Trismus Nascentium ;" possibly an instance of tetany.] Child three days old. Continuous flexion of lower limbs ; inversion of feet ; distortion of features ; fingers variously distorted ; spasm increased by efforts at passive motion. [No trismus mentioned, and] child could suckle and swallow from a spoon. Humeri dislocated forward.

XXIX. 1885. J. Stewart (*Med. News*, 1885, xlvii. 50 ; later, more completely, in *Transac. Assoc. Amer. Phys.*, 1889, iv. 33).—Male, thirty-nine years ; long suffered from chronic diarrhœa. No trace of thyroid gland. Attacks exhibited double vision ; intermittent characteristic spasm of hands, adduction of arms, flexion of forearms ; contraction of facial muscles, and occasionally spasm of lower extremities. Numbness, pain, swelling, and sometimes herpes of hands. Attacks recurred for about ten days. Disease had lasted eight years. Increase of galvanic and of mechanical excitability. No reaction of degeneration. Knee-jerk increased during an attack ; later, absent or weak.

(D.) W. A. Hammond states in a clinical lecture (*N. E. Med. Monthly*, 1885-86, v. 479) that he has seen a few cases ; also, that he is not aware of any cases reported in America.

(E.) G. Ross (*Med. News*, 1885, xlvii. 51) states that he has seen but few cases.

(F.) Godfrey (*Ibid.*, 51) says that he has seen several cases.

XXX. 1886. H. M. Lyman (*Transac. Assoc. Amer. Phys.*, 1886, i. 99).—Delicate man, twenty-eight years. Attacks apt to follow overeating. Spasm of arms and legs, opisthotonos. Respiration sometimes difficult ; occasionally severe headache. Attacks lasted from one to four minutes, and recurred every five to thirty minutes for one or two days, six to eight in a year. Each attack began with forcible beating of right arm against chest.

XXXI. 1886. H. M. Lyman (*Ibid.*).—Nervous man, twenty-two years. Attacks of cramp in left hand, forearm, and sometimes shoulder and side of neck. Intermittent.

XXXII. 1886. H. M. Lyman (*Ibid.*).—Hysterical girl, nineteen years. Exhibited Trousseau's symptom in hand and wrist. [No other note of case.]

XXXIII. 1886. H. M. Lyman (*Ibid.*).—Boy, nine years. Intermittent, painful contractions of flexor muscles of hand and forearm. Fingers flexed over thumb.

XXXIV. 1886. H. M. Lyman (*Ibid.*).—Girl, seven years. Spasm of muscles of neck, arms, hands, feet, and legs, and sometimes of thorax, abdomen, and face. Sometimes laryngismus. Attacks began in hand ; three to fifteen paroxysms a day.

(G.) H. M. Lyman (*Ibid.*) states that he has seen the "milder variety of tetany" in young children usually suffering from diarrhœa ; characterized by flexion of thumbs into palms, often with fingers flexed over them.

XXXV. 1886. A. Jacobi (*Transac. Assoc. Amer. Phys.*, 1886, i. 106).—Young man in whom act of masturbation always brought on attack. Disease did not appear until age of puberty.

XXXVI. 1886. J. T. Carpenter (*Transac. Assoc. Amer. Phys.*, 1886, i. 105 ; later, more exactly, in *Ibid.*, 1889, iv. 44).—Boy, thirteen months ; abscess. Turning of eyes to one side ; typical contraction of arm and hand, first on one side, then on the other ; trismus persistent. All spasm relaxed about third day, then returned ; death in a week. [This case is very powerfully suggestive of tetanus.]

XXXVII. 1887. F. C. Shattuck (*Boston Med. and Surg. Journ.*, 1887, cxvi. 497).—Healthy boy, nineteen years ; had stiffness of jaw for year. This suddenly grew worse, and there appeared numbness, [intermittent (?)] spasm of hands and arms and slightly of legs. Hands in characteristic position. Masseters hard. Pain only on passive movement. Considerable mental excitement. Speech difficult. Trousseau's symptom and increased electrical excitability could not be obtained. Condition relieved in three days under chloral and potassium bromide.

XXXVIII. 1888. H. Hun (*Med. News*, 1888, liii. 415).—Woman, twenty-six years. Suppressed menstruation cause of first attack. Deficient mental power. Disease had lasted two years. At first intermittent spasm, usually in arms and legs ; position of hands and feet characteristic. Later continuous tonic spasm of all the muscles, excepting those of face, persisted even during sleep. Were also paroxysmal painful augmentations of the spasm.

Trousseau's symptom present. Facialis symptom absent. The persistent contraction interfered with the study of the reflexes and electrical reactions. No improvement when case published, after nine months of observation.

XXXIX. 1889. J. T. Carpenter (*Transac. Assoc. Amer. Phys.*, 1889, iv. 45).—Girl, eleven months; suppuration of shoulder. Laryngismus and "muscular contractions of tetany." [The paroxysms were evidently intermittent.] Recovered, but liable for several years to attacks after diarrhœa or taking cold.

(H.) F. P. Kinnicutt (*Transac. Assoc. Amer. Phys.*, 1889, iv. 47) remarked in a discussion upon the subject that he had seen two cases of intermittent tetany in connection with great dilatation of the stomach.

(I.) S. Weir Mitchell (*Ibid.*, 50) said that he had seen but two cases. These may have been Cases XXII. and XXIII., already detailed.

(J.) W. Pepper (*Ibid.*, 51) stated that he had seen only one case, that being in a child.

(K.) A. Jacobi (*Ibid.*, 48) stated that he had met with five cases, and possibly a few more. It may be that one of these was that referred to by him in 1886 (Case XXXV.).

XL. 1889. F. T. Miles (*Transac. Assoc. Amer. Phys.*, 1889, iv. 48).—Woman, twenty-two years. Dilatation of stomach; extreme emaciation. Had had numbness of fingers and toes on several occasions. Developed an attack of tetany with classical position of hands and feet; contraction about face and mouth; rigidity of eyes. Died in twenty-four hours.

XLI. 1889. C. W. Earle (*Transac. Amer. Pædiat. Soc.*, 1889, i. 153).—Girl, two and a half years; indigestion. Characteristic contractions with pain and swelling of hands and feet; muscles of posterior part of legs involved. Spasm continuous. Well in five days. Fomentations and nerve sedatives.

XLII. 1889. C. W. Earle (*Ibid.*). –Girl, six months. Painful continuous spasm and swelling of hands and feet, lasting ten days.

XLIII. 1889. F. C. Shattuck (*Boston Med. and Surg. Journ.*, 1889, cxxi. 231).—Girl, twenty-one years. Diphtheria when sixteen, followed by tetany. At first attacks in one hand and arm, occurred rarely, lasted one to two minutes; gradually all extremities, more frequent, sometimes lasted an hour. Trousseau's symptom present. No inversion of electrical formula.

XLIV. 1889. S. L. Abbott (*Boston Med. and Surg. Journ.*, 1889, cxxi. 230).—Robust 'longshoreman, forty-three years. Spasm of all flexors of extremities, and to some extent of muscles about shoulders and abdomen. Occurred often every half-hour; lasted about a half-minute. Excited by muscular effort. Only slight pain. Improved rapidly under urethan.

XLV. 1889. J. L. Smith (*Arch. of Pædiat.*, 1889, vi. 374).—Boy, eleven months; improperly fed; constipated; one tooth. Had had disease for four months. Spasm [apparently continuous] of muscles in all extremities. Characteristic position of hands. At times spasm of legs and thighs. Attacks of laryngismus. Spasm continued during sleep. Recovered under potassium bromide and relief of constipation.

XLVI. 1889. J. L. Smith (*Ibid.*, 376).—Well-nourished child, twenty months. Dentition thought to have been the cause. Five teeth prominent at once under swollen gums. Flexion of left leg and thigh; [apparently continuous] for three weeks. Spasm present during sleeep.

XLVII. 1889. J. L. Smith (*Ibid.*, 469).—Woman, thirty-nine years. Exposure to wet, cold, and fatigue. Intermittent pain from ankles to knees; in four months, constant; shortly after had continuous flexion of fingers, extension of feet, and flexion of toes. Spasm present during sleep. Sensation in toes nearly lost. Sphincter ani paralyzed for a time. Perspiration of extremities. Spasm of hands well in six months; that of feet still continuing after a year.

XLVIII. 1889. J. L. Smith (*Ibid.*, 472).—Girl, ten and a half months. Severe acute diarrhœa, followed by characteristic spasm of hands and feet with œdema. Several paroxysms during six days, each lasting a day or two, and present during sleep. Had attack of eclampsia on fourth day of disease. Treated with bromides and chloral, and attention to bowels.

XLIX. 1889. J. L. Smith (*Ibid.*, 473).—Boy, fifteen months. Rickets; tendency to diarrhœa; earlier, an inclination to hold breath. Had had nearly continuous characteristic spasm of hands and feet for three months. Spasm present during sleep. Recovery under attention to diet and administration of zinc and atropine.

L. 1890. A. Abrams (*Occid. Med. Times*, 1890, iv. 14).—Man, twenty-four years; excessive smoker; dilatation of stomach. Painless spasms in left arm and sometimes also in left leg;

rarely right arm alone. Sometimes occurred every day at hourly intervals. Violent movements provoked them. Impairment of all forms of sensation in left arm and leg. At times formication and coldness constituted prodromes. Left knee-jerk slightly increased. Trousseau's and Chvostek's symptoms and increase of electrical excitability present. Great exhaustion after attacks.

LI. 1890. J. Schenck (*Journ. Amer. Med. Assoc.*, 1890, xv. 387)—Girl, ten years. Disease had lasted two years. At first vertigo, with spasm of lower limbs; later, only spasm of upper extremities, neck, jaws, and occasionally opisthotonos. Swallowing and speech interfered with; some pain attendant. Hands and arms in classical position. Paroxysms averaged ten daily, each lasting a couple of minutes. Tinnitus, formication, and numbness followed them. Trousseau's and Chvostek's symptoms and knee-jerk absent. Argyll-Robertson pupil present. Disease disappeared in five or six weeks under conium and nitroglycerin.

LII. 1891. E. H. Small (*St. Louis Med. and Surg. Journ.*, 1891, lx. 271; also in several other journals).—Boy, eleven months. Rickets; digestive disturbance. Characteristic continuous spasm, at first painful, of hands and feet, with œdema and cyanosis. In week recovery under fomentations, potassium bromide, and attention to bowels.

LIII. 1892. N. E. Remmen (*Chicago Med. Recorder*, 1892, iii. 240).—Girl, fourteen years. Adenoid growths in naso-pharynx, with poor mental development. Painful spasms of extremities and rigidity of whole body, lasting five minutes and occurring every two months. Disease had lasted two years. Trousseau's and Chvostek's symptoms well marked.

LIV. 1892. S. S. Adams (*Arch. of Pædiat.*, 1892, ix. 881).—Boy, four months; digestive disturbances, phimosis, possibly rhachitis. Laryngismus, and several times eclampsia. Later, "snapping of lids," rolling of eyes, flexion of thumbs into palms, and general rigidity attending laryngismus. These attacks several times daily. Death shortly after from laryngismus.

LV. 1892. W. S. Bowen (*Med. News*, 1892, lx. 434).—Girl, six days old, when she developed attacks of laryngismus with spasm of nearly all muscles of body; opisthotonos and characteristic position of extremities. Lasted about one minute; repeated frequently. [Clearly no trismus. No cause, unless wound left by dropping of cord on fifth day.]

LVI. 1893. B. E. Vaughn (*New York Med. Journ.*, 1893, lviii. 757).—This and the following six cases are instances of epidemic tetany; five of them were in one family; all were Italians living under most unfavorable conditions of dampness and bad air.

Woman, thirty-five years. Nursing; damp, close dwelling. Formication in feet extending to head, neck, and finally hands, with constipation and abdominal pain. Then characteristic spasms in upper extremities, and later in feet, three to four a day, each about one hour. Increased electrical excitability. Disease had lasted three months when first seen. Quinine cured in eighteen hours.

LVII. 1893. B. E. Vaughn (*Ibid.*).—Girl, fourteen years; just beginning to menstruate. Daughter of Case LVI., and developed disease two weeks later. Same exposure to dampness. Formication preceded onset of spasms, which were nearly continuous, relaxing only once or twice a week for a couple of hours. Position of hands and arms characteristic. Rapid recovery under quinine.

LVIII. 1893. B. E. Vaughn (*Ibid.*).—Girl, three years. Rickets; same exposure to dampness as with mother (Case LVI.), and disease began about same time. Spasm in upper extremities twice a week only. Recovery under quinine.

LIX. 1893. B. E. Vaughn (*Ibid.*).—Girl, twelve years. Menstruation recently established; lives in damp house with mother (Case LVI.). Formications, abdominal pain, and constipation as in that case; then continuous characteristic spasm of upper extremities. Trousseau's symptom present. Disease had lasted about two months. Recovered in less than twenty-four hours under quinine.

LX. 1893. B. E. Vaughn (*Ibid.*).—Woman, thirty-three years. Nursing; damp dwelling. Formications, as in Case LVI., for three weeks. Contractions [apparently continuous] began two days before seen. Were increased by pressure on brachial plexus. Disappeared after sixteen grains of quinine in two doses.

LXI. 1893. B. E. Vaughn (*Ibid.*).—Woman, twenty-five years. Damp dwelling; nursing; anæmic, looked sick, had fever and enlarged spleen. Formication as in Case LVI. Contractions [apparently continuous] in fingers and hands began four days before seen. Trousseau's symptom present. Recovered in less than twenty-four hours under quinine.

LXII. 1893. B. E. Vaughn (*Ibid.*).—Man, working in damp place; had typical spasm in both hands and feet.

(L.) B. E. Vaughn (*Ibid.*) states that quite a number of other cases came to the morning Italian class of the New York Dispensary: those reported above having been seen in the afternoon hour.

LXIII. 1893. A. S. Fraser (*Canadian Practitioner*, 1893, xviii. 500).—Man, thirty years. Severe dyspepsia due to cirrhosis of stomach as shown by autopsy. After acute indigestion developed intermittent spasm of muscles of face and extremities, with characteristic position of hands. Spasm lasted one to two minutes; had four in an hour; fifth stopped by puncture with hypodermic needle. Then occasional slight spasms of extremities for some months, with declining health. Then death, preceded by severe spasms of extremities during three days.

LXIV. 1893. J. W. McConnell (*Journ. Nerv. and Ment. Dis.*, 1893, xx. 418).—Woman, thirty-three years. Took general cold. Numbness, pricking, and vague pain, followed by spasm of extremities, neck, abdomen, and zygomatics; tongue stiff, speech and respiration difficult. Muscles alternately relaxed and contracted during about one hour. Voluntary motion increased the spasm. Trousseau's symptom present. A second attack within twenty-four hours.

LXV. 1893. A. Jacobi (*Arch. of Pædiat.*, 1893, x. 1042).—Boy, three years; poorly developed; convulsions at seven months. Fingers bent and thumbs flexed into palms. [Not stated how long this lasted.] Considers chronic meningitis the cause.

LXVI. 1893. A. Jacobi (*Ibid.*, 1055).—Colored child [baby?]; disturbed digestion or exposure apt to be followed by muscular spasms, especially in the hands, with a "peculiar forced position of the limb lasting a day or two." Spasm returning in perhaps a week.

LXVII. 1893. D. J. Evans (*Montreal Med. Journ.*, 1893, xxii. 183).—Girl, seventeen months, colored; rickets. Characteristic spasm of hands and feet, with œdema, continuing ten days, then gradually relaxing. Facial reflex present; knee-jerk exaggerated; no pain. Tonic and dietetic treatment.

LXVIII. 1893. D. J. Evans (*Ibid.*).—Girl, ten months. Chronic diarrhœa, debility, probably syphilis. Five other children had died of convulsions. Continuous spasm of hands and feet, with exacerbations, lasting five days. No facial reflex. Dietetic treatment and potassium bromide.

LXIX. 1893. S. Brown (*North Amer. Practitioner*, 1893, v. 66).—Man, twenty-four years. Exposure to wet and fatigue. Painful spasm in calves and feet, lasting about half an hour, and occurring frequently for three days; worse at night. Increased galvanic excitability. Inversion of formula. Trousseau's symptom absent.

LXX. 1893. S. Brown (*Ibid.*)—Young man. Tingling of whole right side and spasm of right arm, with flexed elbow and closed hand. Spasms lasted one to two minutes, and usually occurred four to five times before breakfast, and occasionally one or more times during the day. Increased galvanic excitability, inversion of formula, and Trousseau's symptom present. Disease had lasted six weeks. Recovery in six days under potassium bromide and galvanism.

LXXI. 1893. S. Brown (*Ibid.*).—Man, twenty-seven years. Exposure to bad weather. Spasm on both "sides" [probably legs meant], lasting several months. [Not stated whether intermittent or continuous.] Says symptoms were well marked, and electrical examination confirmed the diagnosis.

LXXII. 1894. M. H. Fussell (*Univ. Med. Magazine*, 1894, vi. 229).—Girl, five years. Indigestion apt to induce laryngismus and painful characteristic contraction of hands and feet, with flexion of elbows, retraction of head, and strabismus. Spasm continuous during a few days, then disappearing a few days. Exertion made worse; diversion of mind caused nearly to disappear. Trousseau's symptom and knee-jerk absent. Chvostek's symptom present. Disease occurred during several years, especially in spring and fall. Typical epilepsy later in course of case. Death from atelectasis resulting from laryngismus.

Some little analysis of these cases may be of value. Those which offer themselves as at all suitable for this purpose are the ones designated by the Roman numerals. They equal 72 cases in

all. I have not included my own cases in this analysis, since they do not come in the category of those already published.

Conclusions drawn from the cases can only have a relative value, particularly where figures are concerned. This is true both because some doubtful instances of the disease are included in the list, and because many of the reports are incomplete or the meaning of the writers obscure.

In considering the *etiology* of the published cases we find that 34 of the patients were of or above the age of puberty when the disease first developed, including 3 girls in whom menstruation had just been established; 13 were children from two years of age to puberty; 25 were under two years of age, and 20 of these less than one year old.

Sex. 33 of the patients were male, 29 female, and in 10 the sex is not stated.

Among the possible *causes* mentioned or implied, I find lactation (4 cases); open wounds (6); psychic disturbance, including 2 instances of shock from falls (3); menstruation, developing or suppressed (4); possible affection of the brain (3); digestive disturbances, including 2 cases of dilatation of the stomach (23); rheumatism or exposure to cold and wet (13); exposure to heat (1); diphtheria (1); dentition (3); syphilis (1); masturbation (1); absence of the thyroid (1); rickets (5); adenoid growths of the naso-pharynx (1); phimosis (1). Sometimes two or more of these causes were operative in the same case.

Under the heading of *symptomatology* we find it stated that pain in the affected part, apparently due to the spasm, was present in 21 cases, and that it was absent or trivial in 6 cases. In the others no reference is made to the subject. Further, we find among the principal symptoms or complications, faintness (3 cases); vertigo (1); herpes (1); tingling, numbness, formication, etc. (15); temporary paralysis (3); anæsthesia (2); disposition to sleep (1); tinnitus (1); epilepsy (1); laryngismus (17); eclampsia (4). European observers find laryngismus and tetany very frequently associated; and Loos, indeed, has maintained that the former is simply a laryngeal manifestation of the latter disease. Cheadle views laryngismus, tetany, and eclampsia as but different expressions of the same morbid condition. Possibly the association of

tetany with one or the other or both of these allied affections has occurred in America oftener than the reports would indicate. It is interesting to notice that 15 of the 17 cases of laryngismus were witnessed in children under one year of age. Also, that in 11 of the cases the contractions were chiefly continuous and in 6 paroxysmal.

No numerical analysis can be made of the position of the spasm in the body, since it varied from an almost universal diffusion to a limitation to one limb. Trismus was present in probably 6 cases; possibly in a few more in which the reports do not make it quite clear. So, too, it is difficult to draw any conclusions with regard to the nature of the spasm, since we find all gradations occurring, and the writers, too, have not always expressed themselves clearly on this point. As nearly as I can determine the spasm was intermittent, in the sense already defined, in 38 cases and continuous in 25 cases. In 1 case (XIII.) it was at first continuous and later intermittent; in 1 (XXXVIII.) it was first intermittent and then continuous; and in 4 cases (I., VII., X., XXXVI.) it was continuous in one portion of the body and intermittent in another. In 3 cases (LXII., LXV., LXXI.) the authors do not give even a clue to the nature of the spasm.

In only comparatively few cases is there any reference to the presence or absence of Trousseau's symptom and of increased electrical or mechanical excitability as described by Chvostek and Erb respectively.

The *treatment*, so far as it has been reported, has consisted chiefly in remedies employed as sedatives to the nervous system, or directed against the exciting cause of the disease. But very few cases have been fatal, and these only as the result of complications.

Finally, we can but conclude that the cases reported in America entirely uphold the view enunciated earlier in the paper, viz., that there is no essential difference between the tetany of adults and that of children, or between the continuous and the paroxysmal forms of the disease. The cases quoted in considering the nature of the spasm are all in evidence here. Moreover, continued spasm may exist in persons past the age of childhood (Case XVII.), contrary to the statements of some writers; and intermittent spasms, exactly similar to the commoner tetany of adults,

are frequently seen in children. But were there no other instances in proof of the point advanced, the remarkable series of cases published by Vaughn would of themselves be sufficient. Here we find in one family, and at one time, one case (LVI.) of a truly intermittent type, another (LVII.) of a somewhat more continuous form, and a third (LIX.) showing very continuous contraction, yet with Trousseau's symptom present as proof of its true nature.

DISCUSSION.

Dr. W. Gilman Thompson: I have been greatly interested in the report of Dr. Griffith, and I am sure we are all indebted to him for adding so valuable a compilation of these cases to the original ones which he has presented.

I would like to show the photograph of a patient with tetany whom I saw a year ago. He was a male about thirty-five years of age, and his history corresponds so closely to that of the third case reported by Dr. Griffith that it is not necessary to repeat it in detail. The disease lasted about six weeks, and there was absolutely nothing to be determined in regard to its probable cause. The man had been previously in perfect health. He was intelligent, and remained so throughout the disease. The contractions were general, affecting all the muscles of the body, and they included those of the face in a very marked degree, as shown by the photograph. At times they were practically continuous, lasting for many hours, when they would become lessened in severity for a short time. They were intensified by moving the patient and by any voluntary muscular effort. They were exceedingly severe in character and subsided gradually, the muscles of the arms recovering first, those of the legs and trunk next, and those of the face last of all.

Dr. E. G. Janeway: I want to put on record two cases that I have seen in connection with typhoid fever. One in particular was very interesting. It was in a lady of about thirty years of age, who had a very severe attack of typhoid fever, the temperature at times reaching 106°, and the pulse 140 to 150. During the mid-period of the disease, tetany came on in the muscles of the arms and legs, some of those in the back and also those of the jaws, making the matter of feeding a subject of extreme difficulty, so that at times the nurses would be obliged to push down the tongue and lower jaw with a spoon, and then pour in the food with another spoon. It was a question whether we should use a tube, but owing to opposition on the part of the family, we had to resort to the method described. This case was probably

a reflex from the gastro-intestinal tract, though a complication which set in later suggested that it might have come with cystitis, for there was cystitis in which casts of the bladder were discharged. This cystitis came subsequent to tetany. This case showed what might have become a matter of a good deal of difficulty in the diagnosis, because at the time tetany came on other nervous symptoms, owing probably to the high fever, developed and at one time she passed into a condition almost of coma, with Cheyne-Stokes respiration. It is interesting to note that a small injection of morphia to quiet the tetany seemed to help produce the Cheyne-Stokes respiration, and that hypodermic injections of caffeine sodium salicylate relieved it in fifteen minutes. This condition of tetany lasted, as my memory goes, about two weeks, but was severe for only ten days. It made a complication of extreme gravity, and suggested to some who saw her, the possibility of meningitis from the stiffness of the back and neck. The stiffness of the arms and hands gave the clue to tetany and relieved our anxiety a great deal. Another condition that might have produced stiffness of the neck would have been the existence of a sinus thrombosis.

I have seen another case in typhoid in hospital practice. The abstract just presented showed no case of tetany in typhoid fever in this country.

Dr. Charles G. Stockton: I have to report one case of tetany in which the etiology was somewhat obscure, but in which there was one feature that may throw a little light on the subject. It is that of a child, four years old, who was brought to me because he was failing rapidily in strength and flesh, and because he was passing but a small amount of urine. Under my observation, the child developed carpo-pedal spasm, from which he was reported to have suffered before on several occasions during the previous month. This phenomenon continued to a greater or less extent for about two months. There were days when it was scarcely noticeable, but on other occasions it was most marked.

The child had dilatation of the stomach, and lavage was practised with the result of rather lessening than increasing the tetany. At times there was food stagnation, but it was not constant. The singular thing about the case, and that which leads me to report it to-day, was the condition of the urine. At times there was almost complete suppression. For several days together not more than two or three ounces were voided, containing not more than two or three grammes of urea. Occasionally there was seen slight general œdema, but it never persisted long. From the continued scanty urine I was led to believe that I had to deal with a fibro-cystic degeneration of the kidney; but under treatment by baths and gastric lavage there was general improvement; and although this occurred two and a half years ago, the child is still living, and is practically restored to health. I am forced to believe that the kidney disturbance was of functional character. There was at one time albumin in the urine, but no casts were found.

Dr. A. Jacobi: I believe I heard the Doctor say that laryngismus stridulus must be a very rare symptom in America because there were so few reports.

Dr. Griffith: Because of the few reports, and because I and others with whom I have talked rarely meet with it.

Dr. Jacobi: It is our experience in New York—at least it is mine and that of a number of physicians with whose practice I am acquainted, both dispensary and other—that laryngismus stridulus is quite frequent, and when the Doctor said that it must be a rare disease because there are so few reports it struck me that the reverse was the case—that there are so few reports because it is such a common disease. I am sure that in the course of every winter I see at least half a dozen cases of well-marked laryngismus stridulus. Rhachitis is, unfortunately, getting more and more frequent, so are its brain symptoms, and along with them I find laryngismus stridulus. It is very rarely fatal.

Dr. J. J. Putnam: It would seem that tetany must be a pretty rare disease among us. I have the opportunity of seeing in the Massachusetts Hospital some 1200 cases of nervous diseases a year, and I can recall only two really typical cases in adults, and a few instances of the carpo-pedal contractions in infants. Perhaps some other cases, from what Dr. Griffith has said, should be included in the same general category. One of the most interesting of these latter was a continuous trismus in a young lady whom I saw a few times. No satisfactory cause could be assigned. The contraction in her case came and went without our being able to assign any reason for it. I should think it was certainly a disease of this class.

As regards the connection of the carpo-pedal contraction with rickets, we have had good opportunity for the study of rickets from the large number of negroes among us, for the negroes in Boston are very subject to rickets. I have seen one very marked case of carpo-pedal contractions among them, but it is the only case I can recall. I have also seen a case of post-influenzal spasms, where the contractions, which were nearly universal, came on with such severity that the physician who had the patient in charge thought he must have spinal meningitis.

I have also seen a closely similar case associated with severe anæmia after typhoid, where the post-mortem showed nothing but anæmia, both local and general. The contractions simulated opisthotonos.

Dr. William Osler: I will just mention a case which does not come in the etiological category of Dr. Griffith's cases, namely, one occurring in pregnancy, and recurring in six successive occasions. The tetany came on about the sixth month. The case has recently been in my wards, and will be reported in full by Dr. Harry Thomas.

Dr. James Stewart: There appears to be a tendency among the speakers to classify all cases of spasm not attended by tonic loss of consciousness as cases of tetany. Now the genuine tetany described by Trousseau and Weiss is certainly a distinct affection from the vast majority of cases described here to-day. The tetany which is frequently epidemic in Vienna and in some parts of France is an entirely distinct affection from carpopedal contraction. I presume that the word tetany as used at the present time embraces a vast majority of different troubles, and is something like chorea, which is a general term used to signify a great number of different varieties of spasms.

Dr. J. P. Crozer Griffith: In regard to the frequency of laryngismus stridulus I would adopt that view which Dr. Jacobi has expressed, were it not that our experience in Philadelphia has been otherwise. Dr. J. Forsythe Meigs thought it worth while to detail in his well-known text-book of *Diseases of Children* certain cases of laryngismus, as if the disease were rare enough to justify this. Dr. Jacobi's experience shows that the affection is certainly more prevalent in New York City.

Dr. Stewart's view of tetany was the view which I was disposed to adopt when I first commenced the writing of my paper; but the more I looked into the subject the more I found, as my abstracts of cases will show, that it is absolutely impossible to make any sharp distinction between the different conditions which I have included under the one general heading of tetany. There does not seem to be any one distinctive symptom or group of symptoms on which we can base a division between one and the other varieties. After all, perhaps, it seems to me very possible that tetany is a condition, and not a disease; a symptom, a certain expression of a disordered nervous system, just as eclampsia, for instance; or that it occupies a position analogous to that of jaundice. I may say that the definition which I have given expresses practically the definition given by Gowers and by Dana.

STOMATITIS NEUROTICA CHRONICA.[1]

By A. JACOBI, M.D.,
OF NEW YORK.

Case I.—C., fruit business, forty-two years old, married; had one child which was stillborn. His father is alive, seventy-eight years old; his mother seventy five. There are no other relatives except one sister, who is described as being perfectly normal, and one brother, whom I personally know. He appears fairly well developed physically, but has no whiskers, no hair on the pubes, none in the axilla, and the sexual organs are those of a child of ten years. Both of these persons have had pemphigus in the mouth all their lives.

Patient appears to be pretty well developed, his complexion, though, is sallow; all his internal organs are in fair condition. His urine has a specific gravity of from 1.018 to 1.025; is always negative. He has always complained of a sensation of fatigue. He tires very easily, drags his limbs; cohabitation, which occurs but once a month, exhausts him; his hands were always weak, and moderate exertion results in tremor. He has trouble in keeping warm, and complains a good deal of præcordial pain, both on pressure and before his meals. This pain, as he expresses himself, was never so bad as when, under the orders of a physician, his diet was restricted. He has a melancholy temperament, and expresses now and then a number of hypochondriacal notions.

Up to his thirteenth year he suffered severely from urticaria. Since his thirteenth year this urticaria has disappeared, and has been replaced by pemphigus in the mouth. A few blisters will form quite suddenly, sometimes on the tongue, mostly on the cheeks, frequently in their lower parts, near the alveolar processes. They will burst after a little while; whitish ulcers will remain quite a long time and give rise to a great deal of pain,

[1] While this paper was being put in print, Dr. O. Rosenbach published (*Deutsche med. Wochensch.*, June 28, 1894) a paper containing a "Contribution to the Vesiculating Affections of the Oral Mucous Membrane." Its conclusions are as follows: "The local pemphigus of the mucous membrane of the mouth is a variety of erythema exudativum multiforme, and ought to be called erythema bullosum. Whatever has been described as urticaria, herpes, etc., of the oral mucous membrane, is mostly this erythema bullosum. It is often complicated with the same eruption on the genital organs. It has a tendency to relapse."

The very variety of the symptoms, and the etiological identity evidenced in the histories of the cases, makes me believe that the name selected by me is more significant and appropriate.

sometimes resulting in sleeplessness. Half of his lifetime, since his thirteenth year, he has been troubled with this eruption, which would come on without any apparent cause. He states that half of this period he has been free, not being able to explain why he should have the eruption nor why he should have been free.

About ten years ago, after having been under treatment three years, he had no eruption during the course of three or four years. At that time, and in some later periods, the medicinal treatment consisted of the internal administration of atropia, arsenic, and ergot. He claims that no local treatment ever benefited him except the application of concentrated sulphuric acid. He says it was a notion of his own, and asserts that it heals the sores in a few days.

Once, when the patient was as willing as I had been long ago, I sent him to a neurologist of well-merited fame and sound judgment. What he replied was as follows: "I could not make out the cause of the ulcers in C.'s mouth. If it is not a state due to chronic indigestion, and yielding to it, there are two possibilities to consider—one, that he is an epileptic; that the sores are due to attacks in which he bites his cheeks and lips, and of which he is wholly unconscious; secondly, that a morbid tendency leads him to use various acids, etc., in his mouth (and this he admitted he did), which keep up the ulceration or reproduce it. He seemed to me a queer hypochondriacal person, and gave me such an indefinite history that I suspected some mental taint."

Case II.—Mrs. W., thirty-two years old, the oldest of five children in the family. Her father has a very irritable, choleric temperament; her mother is placid, a woman of character and intellect. Her oldest brother has always had a systolic heart murmur, without any hypertrophy, the cause of which can be referred only to an insufficient contraction of the heart muscle. He is now a man of twenty-eight. He has for the last six years had peculiar attacks (epileptic?), the principal symptoms of which are slight contraction of the sterno-cleido-mastoid, which turns his head to the right side; scintillation and semi-unconsciousness, which is sometimes complicated with slight delirium, temporary forgetfulness, and limitation of his field of vision on both sides. These attacks will sometimes come on every month, sometimes not in six months. They are frequently the result of sudden turning of his head in one direction, and upward.

Another brother had meningitis when three years old, with all the symptoms of a tubercular meningitis. The disease did not prove fatal, but from that time on the boy had a feeble intellect, amounting to stupidity; was a bad scholar at school; had an irritable, violent temper, amounting to moral insanity when quite young; became more violent when he grew up, and had finally to be confined in an asylum for the insane, where he has been these many years.

A sister of the patient has suffered from petit mal since childhood, and has feeble intellect, still she is married. A younger sister died when five years old, of convulsions during pneumonia.

Patient was always neurotic; dysmenorrhœa has accompanied her through life; she has been married six years, and has been pregnant four times. The first pregnancy resulted in abortion, the second in the birth of a boy who is four years old and suffers from dyspepsia and constipation. He is a very neurotic boy, cowardly, melancholic, and talks much of his health. The third and fourth pregnancies terminated in abortion.

The patient wore convex glasses, No. 12, twenty years ago; wears No. 6 at the present time. She suffers much from headaches, which do not appear to depend on the condition of her sight. Cephalalgia will come on mostly about the time of menstruation, which is irregular, sometimes scanty, sometimes copious, mostly behind time. Headache will also be produced by reading, thinking, and when the stomach is empty, also under the influence of anxiety or emotions in general. During her headaches she is pale; now and then, however, her forehead will be flushed. Her tendency to constipation will sometimes be interrupted by diarrhœa. Nausea is a frequent symptom; it is often complicated with vertigo. Her kidneys are normal, the urine now and then quite pale and of very low specific gravity.

Other neurotic symptoms are, frequent thirst, also nausea when she stoops and when at work over drawers. In such cases vomiting has been observed which lasted a whole day. Music will confuse her. In the stores she will sometimes forget what she wished to purchase. Occasionally she complains of neuralgic sensations all over the face in every direction. She sees sparks. Whatever she does she complains she does mechanically. She has "to think terribly much."

Whenever she has such attacks of nausea, of vertigo, and during dysmenorrhœa she has a sudden eruption of vesicles in her mouth of a size from a lentil to a pea, preceded by local redness. They burst very soon and leave behind them a sore surface of grayish-white color, which feels a little harder than the normal neighborhood, the hardness evidently depending on a fibrinous exudation into the surface. It takes many weeks before these sores heal. Fortunately they are never numerous. In a number of instances only one would appear. She has had these attacks very frequently since her thirteenth year. Menstruation did not show itself before the fourteenth. The only times when she has been permanently free were during pregnancy and during a trans-Atlantic voyage some four years ago and an absence of about six months.

Case III.—W., stationer, thirty-one years old; never had eczema or other cutaneous diseases; never a chill; has regular bowels; boasts of general good health, and has a great many local and general complaints. He is a good sleeper, his organs appear to be healthy, his urine has a specific gravity of 1.023 and is negative. He smokes but little, but both cigarettes and pipes. Boasts of not being a nervous man. His mother, however, was "quite nervous," and an only sister died of œdema glottidis at the age of thirty-one years. He has been addicted to masturbation from early life until a few years ago. For two years has had attacks of palpitation which last three

or four days, during which breathing is more or less difficult. His heart is of normal size, the sounds feeble; there is no murmur, no hypertrophy. He complains of his stomach, which has been bad three or four years; of slow digestion, and of attacks of vomiting some years ago. He eats rather fast, and takes alcoholic beverages from time to time. The gastric pain he complains of is in the median line. He has it mostly when the stomach is empty. The pain leaves him after eating and returns after an hour or two. His diet does not appear to influence this pain; as he expresses himself, he has pain after everything and is painless after everything.

When he presented himself in March, 1894, he gave the following history: During the last days of 1890 he was sleepless, from no apparent cause. He committed no indiscretion in his diet, but on the 1st of January, 1891, quite suddenly he had what he calls canker sores on his left cheek; blisters sprang up which opened soon and left a white surface which lasted weeks and gave him much pain. He says they travelled around the mouth on both sides, jumping over distances, and have not left him since with the exception of a few days about Thanksgiving Day in 1893. Until that time he had a large number of such blisters and ulcerations of the size of peas and less, rising from what appeared to be a normal surface, on lips and tongue, besides the cheeks. All at once, about Thanksgiving, 1893, he could again whistle and remained well a whole week. Then blisters would spring up again on the outside of the lips; the angles of the mouth cracked, and blisters appeared in the oral cavity, terminating in superficial excoriations. Since the 1st of December, 1893, when the new eruption sprang up, its character has somewhat changed. Besides the large pemphigus vesicles in his mouth, the outside of the lips has participated in the process. There the vesicles are smaller, and rise from a hyperæmic surface. The cheek will swell up now and then, and headaches are not of uncommon occurrence. On April 2d, he complained of a severe headache which had continued a week, and necessitated, and was eased by, prolonged sleep. This headache improved greatly since a few days previous to his call a frontal herpes showed itself. During that time his bowels and appetite had improved, but a symptom which had not been present before and staggered him much, was a very copious perspiration around his anus. On the 17th of May he reported this had disappeared; there was some pain on the right forehead; there was no pemphigus in his mouth, but a few pemphigus eruptions had appeared on the outside of his lips, which had lasted three weeks. He again makes the statement that he has not been free for a year, with the exception of that one intermission in November, 1893.

Pemphigus has amongst its causes heredity and certain affections of the nervous system. Kaposi[1] reports the case of a man of twenty-two years who suffered from pemphigus since his childhood.

[1] A. Eulenburg: Real. Encycl., 2d ed., vol. xx. p. 291.

His sister, his mother, her brother, and half of the children of the latter were similarly affected.

In anomalies of the sexual organs, in pregnancy (Hebra, Bulkley), after confinement (Köbner), it has been observed; in lepra (Boeck, Nielen) it appears either as prodromus and may last for years, or it originates—both traumatically and spontaneously—on anæsthetic parts of the surface. The spinal cord has been found to be altered in chronic pemphigus; it is met with in chronic myelitis and in neuritis. But in all of these cases pemphigus was not found on the mucous membrane, as in those related by me, and the following:

Kopp[1] describes a case of what he calls tropho-neurosis hysterica. It was that of a woman with a neurotic history and hysterical attacks. Amongst other eruptions she had herpes on the lower lip over the right mental nerve, and after that a small vesicle over the middle of the upper lip. This was followed by a large vesicle on the left side of the lower lip and a stomatitis with frequent hysterical attacks. Both vesicles and stomatitis disappeared in five days. Later on there was marked pain in the gums and on the mucous membrane of the mouth, followed by herpetic vesicles on the lower lip and a marked stomatitis, with fetid breath and frequent hysterical attacks. A week later there came another crop of herpetic vesicles on the lower lip, and the same condition would repeat itself at longer or shorter intervals. During all these attacks the temperature was normal. Alongside the vesicles there went a desquamating catarrh of the mucous membrane of the mouth, which recurred frequently and suddenly. Some months afterward, with a recurrence of the hysterical attacks and other skin affections, there was again herpes on the lips as before, and a marked stomatitis.

T. S. Flatau publishes,[2] under the head of chronic recurrent herpes of the oral cavity, the case of a merchant, thirty-eight years old, who was well until his eighteenth year. Then he had typhoid fever and became addicted to alcohol; it is thus that the neurotic element may be surmised to have come into the case. Some months after his convalescence from typhoid fever he had an herpetic eruption on the lower lip, which soon healed. Since that time he frequently had similar eruptions on the mucous membrane of the

[1] Trophoneurosen der Haut. Inaug. Diss., Würzburg, 1891.
[2] Deutsche med. Wochenschr., 1891.

lips, on the gums, near the floor and roof of the mouth, occasionally also on the tongue, mostly along the free margin posteriorly. These crops would last from eight to twenty-eight days. The longest time that he was ever free was one year, being then also relieved of the general irritability of his nervous system. Then the eruptions reappeared, and since that time the intervals between them have continually grown shorter. It was also observed that when his nose was clear there was no eruption, and when the latter appeared the nose was obstructed. He never had neuralgic pains, but salivation frequently. Patient shows marked mental depression, which he explains by the fact of his suffering from his trouble through so long a period and his impossibility to master it by treatment. There was no syphilis, no tuberculosis, no malaria. The simultaneous appearance of nasal symptoms might suggest a causal influence of the latter, but it is quite as probable that the mucous membrane of the mouth and of the nose was affected at the same time. But there is no means of arriving at a correct diagnosis of the original condition. The assumption of a peripheral or central affection of the trigeminus is hypothetical.

B. Mandelstamm[1] observed four cases of pemphigus of the mucous membrane of the mouth within ten years. In one of them the eruption was also seen part of the time on the skin. In all of them the treatment was unavailing. There was no systemic disturbance, but there was fetid breath and painful deglutition. Eruptions were found on the mucous membrane of the tongue, cheek, lips, and throat. The sores were of a size from a lentil to a cent. They were grayish-white or white. The patches had sharply defined borders. Some were thick, like a membrane, and could not be removed without leaving a bleeding surface. The eruptions, when on the tongue, were usually found on the free border of the inferior surface. Now and then they would appear on the epiglottis. Around the excoriations or membranes there was usually slight œdema, and salivation was not uncommon. Microscopic and bacteriological examinations were all negative.

The author has scanned the literature quite carefully, and comes to the conclusion that such cases must be very rare. A little more

[1] Berl. klin. Wochenschr., 1891.

frequent are detachments of epithelium which remain membrane-like on the surface, and may resemble to a certain extent diphtheritic or croupous membranes.

With the exception of a few cases to be mentioned hereafter, the above cases of chronic pemphigus of the mouth appear to be all that have been observed. A few instances of pemphigus of the skin I now propose to mention briefly, and to accompany them with a very few remarks which are meant to elucidate the peculiar etiology of the affection.

Kirchner's case[1] was that of a man of fifty-four years, who was reported to have had a primary specific affection without, however, exhibiting secondary symptoms. For the past seven years he was frequently taken with pemphigus eruptions on arms, legs, face, and neck, accompanied with general systemic disturbance and sweating. Sudden exposures to cool air after perspiration were presumed to occasion the attacks. At the Ninth Congress[2] of Internal Medicine a few cases of pemphigus were the subjects of discussion. Mosler claimed it as a vasomotor, Schwimmer as a trophoneurotic affection; as to its neurotic character there appeared to be no doubt. As the suspicion of its being of an infectious nature easily suggests itself, microbes were carefully looked for by Mosler, but not found. Nor was Landgraf more successful in this respect, in a case of chronic pemphigus of the conjunctivæ and the mucous membranes of the nose, fauces, and oral cavity.[3] A similar case was reported by Boer[4] and Chiari;[5] it was observed in a coachman of sixty-three years, who developed pemphigus on the mucous membrane of the larynx. Tuberculosis was suspected, but the diagnosis was dropped when subsequently the same eruption showed itself on the throat and mouth. No attempt is made in the publication to diagnosticate the cause.

Mosler's case in a woman of thirty, of pemphigus of the skin of the trunk and extremities, was decidedly of a neurotic character, in a neurotic family. The patient was always of delicate health, and had repeated attacks of epistaxis, fainting, and epilepsy from her twelfth to her fifteenth year; afterward she suf-

[1] Archiv f. Dermatol. u. Syph., Wien, 1892.
[2] Verhandl., Wiesbaden, 1890, p. 252.
[3] Berl. klin. Wochenschr., 1891.
[4] Archiv f. Dermatol. u. Syph., 1890.
[5] Wiener klin. Wochenschr., 1893.

fered from chlorosis, dysmenorrhœa, arthritis, hæmoptysis, and hæmatemesis.

Benedict observed pemphigus both after peripheral nerve lesions and central disturbances. So have Charcot, Leyden, and Eulenburg. Hebra quotes Dickson and Gilibert, who claim emotional excitement as amongst the causes of pemphigus, and admits the existence of a "pemphigus hystericus" which appears and disappears in combination with a series of hysterical symptoms. A unilateral case of the kind is reported by Pick (*Wiener med. Presse*, 1880).

The majority of the neuroses of the integuments, which result either in a simple hyperæmia and œdematous tumefaction or in exudation reaching up to and into the epidermis, have been described as either urticaria or herpes. They are found on the skin almost exclusively. In severe generalized urticaria of the surface I have, however, repeatedly met with an œdematous swelling of the mucous membrane of the mouth; once I observed an acute laryngeal catarrh with croupous cough and dyspnœa, and once a very intense rectal tenesmus. Herpes febrilis I have seen quite often, when severe on lips and chin, to spread over tongue and cheeks, exhibiting the same character in all localities, and following the course of a peripheral branch of the trifacial nerve. As a rule, however, both urticaria and herpes are limited to the surface. Hemorrhages into the skin I have now and then found in exquisitely hysterical women. Pemphigus, as the literature of the subject proves, is but rare in that connection. Whenever found, it is on the skin almost exclusively, not on the mucous membrane. With the exception of the few cases given in detail, there are amongst the instances quoted above only those of Landgraf, Boer, and Chiari in which pemphigus was limited to the mucous membrane of the oral cavity.

Herpes is by no means rare; indeed, *acute* herpes ("zoster") is a frequent neurosis. Its form, however, is not always the same. In some eruptions of zoster the liquid exudation does not suffice for the formation of vesicles; in others the vesicles are very large, like those of pemphigus. These two varieties of dermatitis will sometimes resemble each other in many points. Mosler's case of cutaneous pemphigus began with small vesicles; within four or six hours they were of the size of pigeon's eggs. In one of my cases the pemphigus eruption was surrounded with a hyperæmic area, and that

of Kopp's is of a similar nature. These instances prove the at least occasional presence of equal etiological and pathological conditions. Still, the great scarcity of pemphigus of the mucous membrane of the mouth appeared to me a sufficient reason both to describe my cases and to range them under a special heading. The neurotic character of my cases appeared to me self-evident. In two there is a positive family taint; in one the taint is but individual, but the neurosis finds its cause, amongst others, in masturbation, and exhibits a series of nerve anomalies. Even gastric symptoms, when they occurred in my cases, were easily recognized as neurotic. Other symptoms of the same nature were headaches, constipation, diarrhœa, nausea, local perspiration, and general neurasthenia. The temperature of the body was always normal. Contrary to what we see in herpes of the surface, which heals readily unless maltreated, pemphigus of the mouth is of long standing, and heals but slowly, and gives rise to a great deal of protracted pain and discomfort.

The marked family disposition which is evident in the history of two of my cases, reminds me strongly of what Carl Blumer has described under the heading of "hereditary disposition to vesiculation" (Prague, 1892). Valentin employed for the same affection the name of hereditary dermatitis bullosa; Köbner called it epidermolysis bullosa hereditaria; and Klebs, dysplasia vasorum. He found the bloodvessels in a condition resembling that of hæmophilia; down to the capillaries they consisted pre-eminently of cells of embryonal structure, predisposing to hemorrhages and exudation. Some of the cases described by Blumer and others (Goldscheider, Valentin, Ferd. Hebra, and Köbner) were complicated with urticaria, swelling of the lymphatic vessels and lymph-bodies, tumefaction and redness of skin surrounding the vesicles, general malaise when eruptions were copious, hemorrhages into the vesicles, suppuration, and purpura.

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